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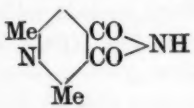
917	9*	atomic number of tungsten, *for* "76" *read* "74."

* From bottom.

CC.—*Synthetical Experiments in the Naphthyridine Groups.*

By JOHN MASSON GULLAND and ROBERT ROBINSON.

THE sodamide method of Tschitschibabin (*J. Russ. Phys. Chem. Soc.*, 1914, **46**, 1216; 1915, **47**, 835) has rendered many α- and γ-aminopyridine derivatives readily accessible, but it is still difficult to obtain β-aminopyridines in quantity. We have utilised the fact that 2 : 6-dimethylcinchomeronic acid is easily prepared (Mumm and Hüneke, *Ber.*, 1917, **50**, 1568) in devising a method of preparation of 3-amino-2 : 6-lutidine (III). 2 : 6-Dimethylcinchomeronimide (I), obtained from the acid by heating with carbamide (compare Herzog, *Z. angew. Chem.*, 1919, **32**, 301; Lawson, Perkin, and Robinson, J., 1924, **125**, 634), is converted by potassium hypobromite and potassium hydroxide into a salt of 3-amino-2 : 6-dimethyl*iso*nicotinic acid (II). This acid yields the aminolutidine on distillation with soda-lime. The product is quite different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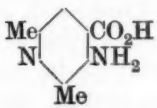
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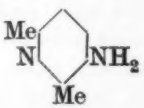
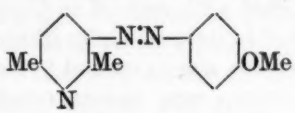
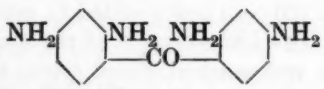
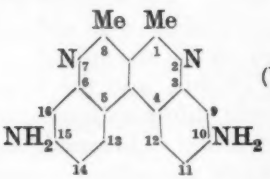

(III.)

from 4-amino-2 : 6-lutidine (Marckwald, *Ber.*, 1894, **27**, 1325), and this fact establishes the constitution of the new base. We have made many fruitless attempts to convert this aminolutidine into 1 : 7-naphthyridine derivatives, for example, by condensation with acetylacetone and by application of the Doebner-Miller synthesis. The reactivity of the nucleus appears to be feeble. The diazonium salt derived normally from the base couples with phenol with formation of lutidineazophenol, the *O*-methyl ether (IV) of which was examined by the method of Jacobson for the semidine transformation on reduction. No evidence of this was obtained, and as regards the benzidine transformation, Friedl (*Monatsh.*, 1913, **34**, 765) has prepared 3-hydrazopyridine, but makes no mention of a molecular rearrangement of this substance. Intramolecular changes of these types are clearly not facile in the pyridine series.

(IV.) 

(V.) 


(VI.)

The copyrine synthesis from derivatives of *oo*-diaminobenzophenone and 1 : 3-diketones described by Lawson, Perkin, and Robinson (*loc. cit.*) involves a very satisfactory reaction from the point of view of yield and convenience, but the number of available diaminobenzophenones is limited. We have now obtained 2 : 4 : 2′ : 4′-*tetra-aminobenzophenone* (V), and from it, by condensation with acetylacetone, a *diaminodimethyldibenzocopyrine* (VI).

Further brief indications of synthetical schemes will be found in the experimental section.

Experimental.

2 : 6-*Dimethylcinchomeronimide* (I).—In the preparation of 2 : 6-dimethylcinchomeronic acid (Mumm and Hüneke, *loc. cit.*) the isolation of the ester was found to be unnecessary. The product of the condensation of ethyl acetylpyruvate (83 g.) with ethyl β-aminocrotonate (69·3 g.) in ether (40 c.c.) was, after 15 hours, hydrolysed with potassium hydroxide (25 g.) dissolved in 70% alcohol (150 c.c.). Following steam distillation, the liquid was acidified with respect to Congo-red, and sodium acetate added to neutralise the mineral acid. The acid, m. p. 274° (pure 275°), crystallised from the solution in quantitative yield. The conversion into the *imide* by heating the ammonium salt at 230°, as described by Mumm and Hüneke, is troublesome, and the following process is far more convenient. The acid (10 g.) and carbamide (5 g.) were heated together with stirring at 225° until ammonia was no longer evolved (about 5 minutes), then at 230° for a few moments, and the mass was cooled and extracted with alcohol. The substance, m. p. 230° (Mumm and Hüneke give m. p. 230°), crystallises from the solution in yellow needles (yield 81%).

3-*Amino*-2 : 6-*dimethylisonicotinic Acid* (II). (Compare Gabriel and Colman, *Ber.*, 1902, **35**, 2832, for the preparation of 3-amino-*iso*nicotinic acid from cinchomeronimide).—Finely-powdered 2 : 6-dimethylcinchomeronimide (20 g.) dissolved when it was gradually added to a well-stirred, ice-cold solution of potassium hypobromite prepared from bromine (18·2 g.) and 10% aqueous potassium hydroxide (300 c.c.). After 2 hours, 10% potassium hydroxide (160 c.c.) was added and the mixture heated for 10 minutes on the steam-bath. The solution was acidified with respect to Congo-red with hydrochloric acid and evaporated to dryness under diminished pressure on the steam-bath. The residue was extracted twice with boiling alcohol, and the filtered solutions were concentrated to a small bulk, dilute hydrochloric acid (20 c.c.) being added to prevent the separation of inorganic salts. The *hydrochloride* of the amino-acid, which crystallised on cooling, was washed, dried (yield 16 g.

or 60%), and recrystallised from dilute hydrochloric acid, separating in slender, pale yellow needles, decomp. 248° (Found in material dried over sulphuric acid: Cl, 14·9; loss at 110°, 8·4; loss at 130°, 15·2. $C_8H_{11}O_2N_2Cl,2H_2O$ requires Cl, 14·9; $1H_2O$, 7·6; $2H_2O$, 15·1%). The long, yellow needles which separate from alcohol have m. p. 253—255° with previous slight darkening. This salt is readily soluble in water and sparingly soluble in dilute hydrochloric acid. The amino-group can be diazotised and coupling with β-naphthol produces a red azo-compound.

Sodium acetate was added to a concentrated aqueous solution of the hydrochloride, and the pale yellow, oblique-ended prisms of the *acid* which slowly separated were washed, and dried over sulphuric acid (Found: loss at 110°, 5·1; in material dried at 110°, C, 57·9; H, 6·1. $C_8H_{10}O_2N_2,0{\cdot}5H_2O$ requires H_2O, 4·9. $C_8H_{10}O_2N_2$ requires C, 57·8; H, 6·0%). The acid is sparingly soluble in neutral organic solvents, more readily soluble in water, and easily soluble in alcohol; it melts at 295° after darkening at 285°. The *copper* salt occurs in yellow, prismatic needles, moderately soluble in water, and the *lead* salt in colourless, quadrilateral or hexagonal prisms which do not melt at 315°.

3-*Amino*-2 : 6-*lutidine* (III).—A mixture of the hydrochloride of aminodimethyl*iso*nicotinic acid (15 g.) with powdered soda-lime (5 parts) was strongly heated in a combustion tube in a stream of hydrogen. The distillate, which solidified (6·4 g.), crystallised from benzene in colourless needles, m. p. 122°, and from water in needles which melted indistinctly between 70° and 75° and lost 14·4% on drying over potassium hydroxide in a vacuum; they then melted at 122° (Found: C, 68·7; H, 8·4; N, 22·9. $C_7H_{10}N_2$ requires C, 68·8; H, 8·2; N, 22·9% and $C_7H_{10}N_2,H_2O$ requires H_2O, 14·7%).

This strong base has a characteristic odour and is readily soluble in most organic solvents, although somewhat sparingly soluble in ether. The *hydrochloride* is very readily soluble in water and separates from alcohol in flat needles, m. p. 235°.

3-p-*Hydroxybenzeneazo*-2 : 6-*lutidine* (corresponding with IV).—3-Aminolutidine (4·2 g.) was diazotised below 2° in hydrochloric acid (13·7 c.c.; *d* 1·16) and water (80 c.c.) with sodium nitrite (3·6 g.) in water (50 c.c.). The diazo-solution was slowly added to a cold, agitated solution of phenol (3·2 g.) and sodium hydroxide (6·9 g.) in water (100 c.c.), and, after 5 minutes, the dark red solution was saturated with carbon dioxide. The orange-brown precipitate, after being washed and dried (yield 6·7 g. or 86%), crystallised from toluene in flat, orange needles, m. p. 240° (decomp.) (Found in material dried at 110°: C, 68·9; H, 5·9; N, 18·6. $C_{13}H_{13}ON_3$ requires C, 68·7; H, 5·7; N, 18·9%). The substance is sparingly

soluble in ether, benzene, or chloroform, and is moderately readily soluble in alcohol, acetone, or ethyl acetate. The solutions in concentrated sulphuric and hydrochloric acids are bright red and the *hydrochloride* crystallises from dilute hydrochloric acid in orange-yellow needles, m. p. 239—240° (decomp.) (depressed by admixture with the base). In caustic alkalis, an orange-red solution is obtained, but the compound is less readily soluble in aqueous ammonia than benzeneazophenol.

The *methyl* ether (IV), which could not be obtained by the action of methyl sulphate on the phenol, since methylation of the tertiary nitrogen atom ensued, was prepared by Pyman's method (J., 1918, **113**, 227) for the *O*-methylation of phenolic bases; the conversion of benzeneazophenol into benzeneazoanisole by this process was found to be 75%. The lutidineazophenol (2 g.) and sodium methyl sulphate (3·6 g.; 3 mols.) were added to a solution of sodium *iso*amyloxide (from 0·2 g. of sodium) in *iso*amyl alcohol (20 c.c.), and the mixture was boiled under reflux for 2 hours, the colour changing from red to dark brown. Ether and dilute sodium hydroxide solution were added to the cold mixture, and the ethereal layer was washed with dilute alkali and water, filtered, and the solvent removed by distillation and steam distillation. The residue crystallised on cooling (yield 1·86 g. or 87·7%); 0·25 g. of unchanged phenol was recovered. *Lutidineazoanisole* is rather readily soluble in organic solvents and crystallises from light petroleum in elongated, diamond-shaped, red plates, often forming radiating clusters; it melts at 81—82° and solidifies to a yellow mass on cooling. When the bright red crystals were collected, they became yellow in places, but the change did not progress on keeping (Found: C, 69·6, 69·4; H, 6·2, 6·2. $C_{14}H_{15}ON_3$ requires C, 69·7; H, 6·2%). The *hydrochloride*, orange needles, sparingly soluble in dilute hydrochloric acid, melts to a paste at 112°, but, after drying at 100°, has m. p. 183—185° (decomp.). The semidine transformation was attempted by treatment of the ether both with acid reducing agents, such as alcoholic stannous chloride and hydrochloric acid, and with neutral reducing agents, such as aluminium–mercury and alcohol, and hydrogen in presence of palladium, followed by treatment with acids. The products gave no trace of triazole derivatives on treatment with nitrous acid. The failure of the semidine rearrangement also involved the breakdown of an otherwise feasible synthesis of harmine.

Derivatives of 3-Amino-2-methylcinchoninic Acid.—The object in view in making the experiments described below was the conversion of the accessible 3-amino-2-methylcinchoninic acid (Lawson, Perkin, and Robinson, *loc. cit.*) into a 1 : 7-naphthyridine derivative

by applying the Camps synthesis of 2 : 4-dihydroxyquinoline from anthranilic acid (*Arch. Pharm.*, 1899, **237**, 659). The attempt was abandoned on account of the difficulties encountered, and indicated in the sequel, but also because Seide (*Ber.*, 1924, **57**, 1806) failed to obtain a naphthyridine derivative in a similar manner from 2-aminonicotinic acid.

Methyl 3-*Amino*-2-*methylcinchoninate*.—The acid is not esterified when its solution in dry methyl alcohol (25 g. in 500 c.c.) is saturated with hydrogen chloride and heated under reflux for 3·5 hours. This phenomenon is not abnormal, since the conditions for the exercise of powerful steric hindrance are present, whilst, in addition, the basic character of the substance operates against the exhibition of oxonium character by the oxygen atoms of the carboxyl group.

A mixture of the acid (10 g.), sulphuric acid (10 c.c.), and methyl alcohol (100 c.c.) was boiled under reflux for 7 hours. Barely 1 g. of the *ester* was ultimately isolated as a viscous, yellow oil which soon solidified; it crystallised from light petroleum (b. p. 60—80°) in canary-yellow needles, m. p. 83—84° (Found : C, 66·4; H, 5·6. $C_{12}H_{12}O_2N_2$ requires C, 66·7; H, 5·6%). The substance exhibits brilliant blue fluorescence in ethereal solution, and is readily soluble in dilute hydrochloric acid and most organic solvents. The *acetyl* derivative was apparently not produced by the action of boiling acetic anhydride alone, but when the ester was boiled with an excess of acetic anhydride and fused sodium acetate for 10 minutes a substance was isolated in about 35% yield, which crystallised from benzene–light petroleum in pale yellow needles, m. p. 169°. This is doubtless *methyl* 3-*acetylamino*-2-*methylcinchoninate*, but the method of preparation is very unsatisfactory and attempts, unfortunately fruitless, were made to reverse the order of the operations. 3-*Acetylamino*-2-*methylcinchoninic acid*. A mixture of amino-methylcinchoninic acid (10 g.), fused sodium acetate (10 g.), and acetic anhydride (30 c.c.) was gently heated over a free flame until a vigorous reaction set in and the yellow colour disappeared. After being heated to incipient ebullition for a minute, the product was cooled, decomposed with water, and the precipitate collected and dried (10 g.). The material was a mixture, and an acidic fraction was separated from a neutral fraction (A) by means of dilute aqueous sodium carbonate. The acid precipitated from the filtered alkaline solution was at first gelatinous, but became crystalline when the mixture was heated on the steam-bath for about 10 minutes. The substance crystallises from much hot water in small, colourless needles which, after drying in a vacuum, lose 10·3% at 100° and then have m. p. 286° (Found in material dried at 100° : C, 64·2; H, 4·9. $C_{13}H_{12}O_3N_2,1{\cdot}5H_2O$ requires H_2O, 9·6% and $C_{13}H_{12}O_3N_2$

requires C, 63·9; H, 4·9%). This compound is sparingly soluble in most organic solvents, but dissolves in dilute hydrochloric acid at about 40° and separates again on cooling. The acetyl group was not removed when a solution of the substance in dilute aqueous sodium hydroxide was boiled for 4 hours; a sodium salt separated in silky needles from the cooled solution and by treatment with dilute acetic acid gave the unchanged acid, m. p. 286°.

A curious result followed an attempt to esterify the acid. A mixture of 3-acetylamino-2-methylcinchoninic acid (2 g.), sulphuric acid (3 c.c.), and methyl alcohol (20 c.c.) was boiled under reflux for 3·5 hours. After distillation of half the methyl alcohol, the mixture was added to water and ammonia and extracted with ether, which removed nothing. The ammoniacal solution was then acidified with hydrochloric acid and, on keeping, 1·9 g. of a yellow substance separated which crystallised from water in feathery, yellow needles, m. p. 217° (decomp.) [Found: loss at 100°, 14·3; in material dried at 100°, C, 64·8; H, 5·1. $C_{24}H_{22}O_5N_4(2C_{11}H_{10}O_2N_2 + C_2H_4O_2 - H_2O)$ requires C, 64·6; H, 4·9% and $C_{24}H_{22}O_5N_4,4H_2O$ requires H_2O, 13·9%). When the acetylamino-acid was boiled with concentrated hydrochloric acid it was quickly converted into an acid, devoid of basic properties, which, crystallised from dilute hydrochloric acid and then from alcohol, formed bright yellow needles, m. p. 234—235° (Found in material dried in a vacuum: loss at 100°, 5·6; in material dried at 100°, C, 63·1, 63·4; H, 5·5, 5·6; N, 12·8%). Both substances, m. p. 217° and m. p. 234—235°, are acids which are readily soluble in aqueous sodium carbonate, and the latter was shown to be unaffected by boiling dilute aqueous sodium carbonate in ½ hour. We have not reached any definite conclusion as to the nature of these substances.

Anhydro-3-acetylamino-2-methylcinchoninic Acid.—The material (A) obtained in the course of the acetylation of aminomethylcinchoninic acid crystallised from alcohol or benzene in colourless needles, m. p. 199—200° (Found: C, 69·1; H, 4·6; N, 12·2. $C_{13}H_{10}O_2N_2$ requires C, 69·0; H, 4·4; N, 12·4%). On boiling with water, the substance is slowly hydrated, but more rapidly in presence of sodium hydroxide, with the formation of 3-acetylamino-2-methylcinchoninic acid, m. p. 286°. The substance resembles acetylanthranil (compare Schroeter and Eisleb, *Annalen*, 1909, **367**, 124), and its constitution is probably analogous (O instead of NPh) to that of the pyrimidine derivative described below.

1-Keto-2-phenyl-3 : 5-dimethyl-1 : 2-dihydro-2 : 4 : 6-naphthaisotriazine, $C_9H_4MeN<\begin{matrix}CO\cdot NPh\\ |\\ N{=}CMe\end{matrix}$.—A mixture of anhydro-3-acetylamino-2-methylcinchoninic acid (0·7 g.) and aniline (2 c.c.) was

boiled for 2 minutes and cooled, and the product was washed with alcohol and crystallised from much alcohol, separating in yellow needles, m. p. 235° (Found: C, 75·6; H, 5·3. $C_{19}H_{15}ON_3$ requires C, 75·7; H, 5·0%). This sparingly soluble substance is a weak base and is precipitated unchanged on addition of water to its solution in concentrated hydrochloric acid.

2 : 4 : 2′ : 4′-*Tetra-aminobenzophenone* (V).—Schöpff's method of tetra-nitration of diphenylmethane (*Ber.*, 1894, **27**, 2318) resulted in inferior yields, and the following method effected a considerable improvement. Molten diphenylmethane (53 g.) was added drop by drop to a stirred solution of potassium nitrate (128 g.) in sulphuric acid (360 g.) maintained below 25°. An equal quantity of potassium nitrate was then introduced and the mixture frequently shaken and heated on the steam-bath for 30 minutes. The isolation was by the method of Schöpff, and the yield 70%. The oxidation of tetranitrodiphenylmethane with chromic and acetic acids as described by Städel (*Annalen*, 1883, **218**, 341) proved a most unsatisfactory process and, after numerous trials, we finally adopted the following conditions. Tetranitrodiphenylmethane (10 g.) was dissolved in concentrated sulphuric acid (90 g.) and water (10 g.), and a concentrated aqueous solution of chromic acid (5·8 g.) added with vigorous agitation, the temperature being maintained below 40°. The mixture was finally heated for an hour on the steam-bath, added to water, and the precipitate collected and dried (7·5 g. or 72%). A specimen crystallised from acetic acid melted at 224—225° and for ordinary purposes the crude product can be satisfactorily purified by extraction with hot ethyl acetate. A good criterion of purity is the absence of the blue coloration with alcoholic potassium hydroxide which is so characteristic of tetranitrodiphenylmethane.

The tetranitrobenzophenone (10 g.) was suspended in a mechanically stirred mixture of acetic acid (100 c.c.) and concentrated hydrochloric acid (65 c.c.), and granulated tin (45 g.) gradually added. After about 20 hours, the liquid contained no solid nitrocompound in suspension and gave a clear solution with water. Sufficient water to dissolve the tin salt was added, and the filtered solution rendered strongly alkaline by the addition of sodium hydroxide. After a few hours, the black sludge and yellow needles were collected, dried, and extracted several times with hot alcohol. Dull, yellow prisms (3 g.) separated on cooling the concentrated extracts; the base, recrystallised from alcohol, had m. p. 202° (Found: C, 64·5; H, 6·0; N, 23·2. $C_{13}H_{14}ON_4$ requires C, 64·5; H, 5·8; N, 23·1%). Tetra-aminobenzophenone is readily soluble in acetone, ethyl acetate, or methyl alcohol, sparingly soluble in

benzene or chloroform, and very sparingly soluble in ether. Just above its m. p. the substance evolves ammonia; the residue dissolves in dilute hydrochloric acid, the yellow solution exhibiting bluish-green fluorescence. This behaviour indicates the formation of diaminoacridone. On treatment of an acid solution with sodium nitrite, a brown precipitate is thrown down and the solution contains a diazonium salt.

10 : 15-*Diamino*-1 : 8-*dimethyldibenzocopyrine* (VI). — Concentrated hydrochloric acid (5 c.c.) was added to a mixture of 2 : 4 : 2′ : 4′-tetra-aminobenzophenone (1 g.), acetylacetone (1 g.), and water (25 c.c.), and the whole gently heated. In about ½ minute orange crystals separated and the mixture was then boiled for a minute and cooled. The crystals were collected, washed with alcohol, and dried in a vacuum (Found: Cl, 26·6. $C_{18}H_{16}N_4,3HCl$ requires Cl, 26·7%). This *hydrochloride* occurs in orange-red, rectangular plates, which decompose without melting at 310°. It crystallises in beautiful leaflets when hydrochloric acid is added to an aqueous solution. The yield in the preparation is almost quantitative if account be taken of the small amount of base recoverable from the original filtrate. In order to obtain the free base, the salt was dissolved in boiling dilute acetic acid and potassium hydroxide added until crystals began to separate. The heating was then discontinued and the remainder of the base precipitated by the further addition of potassium hydroxide. The substance was collected, washed, dried, and dissolved in a large volume of hot alcohol (charcoal). The filtered solution was concentrated by distillation and, at a certain stage, pale brown cubes were deposited from the hot solution (Found: C, 75·2; H, 5·6; N, 19·2. $C_{18}H_{16}N_4$ requires C, 75·0; H, 5·6; N, 19·4%). The substance is sparingly soluble in most organic solvents and its alcoholic solution exhibits a weak green fluorescence. It begins to decompose at about 305°, but does not melt at 340°. The base can be normally tetrazotised and coupled with β-naphthol to produce a crimson azo-compound.

An attempt to shorten the preparation was made, the product of reduction of tetranitrobenzophenone (1 mol.) being treated with zinc to eliminate tin and then with acetylacetone (3 mols.) on the steam-bath. After the red precipitate had been treated with successive quantities of cold alcohol, the residue consisted of the above-mentioned trihydrochloride. The alcoholic filtrates were evaporated to dryness; the residue crystallised from dilute hydrochloric acid in dark red needles which, air-dried, lost 19·6% at 130°, leaving a purplish-brown mass with a green reflex. This salt exhibits a most brilliant green fluorescence in solution and contains a diazo-

tisable amino-group. The amount of material at our disposal did not permit of further investigation.

Benzoylveratroylmethane, $PhCO{\cdot}CH_2{\cdot}CO{\cdot}C_6H_3(OMe)_2$. — Ethyl veratrate (10·5 g.) and acetophenone (7·5 g.) were condensed together by means of granulated sodium (2·3 g.) under dry ether (50 c.c.), and the diketone was isolated as the *copper* salt (5 g.) in the usual manner. This substance crystallised from benzene in pale green leaflets, m. p. 250° (Found: Cu, 10·1. $C_{34}H_{30}O_8Cu$ requires Cu, 10·1%). The *benzoylveratroylmethane* obtained by its decomposition with dilute sulphuric acid in presence of ether crystallised from methyl alcohol in pale yellow plates, m. p. 67°, and was readily soluble in most organic solvents (Found: C, 71·7; H, 5·6. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·6%). An alcoholic solution is coloured greenish-brown on the addition of ferric chloride.

Ethyl Benzoylveratroylacetate, $(MeO)_2C_6H_3{\cdot}CO{\cdot}CH(CO_2Et){\cdot}COPh$. —As the yield of benzoylveratroylmethane was rather poor in the direct process, this ester was prepared, but it could not be hydrolysed so as to yield the desired product.

Solutions of sodium ethoxide (from 8·7 g. of sodium) in alcohol (147 c.c.) and of veratroyl chloride (39·5 g.) in benzene (500 c.c.) were prepared. Half the sodium ethoxide solution was added to ethyl benzoylacetate (37·8 g.), and the mixture stirred and cooled to 0°. Half the veratroyl chloride solution was added during 15 minutes, and the mixture allowed to remain for 30 minutes. The cycle of operations was repeated several times, on each occasion one-half of the volume of the solution which remained being added. After 12 hours, the dense, yellow precipitate of crude sodium salt was collected, washed with benzene, dried in the air, and decomposed in aqueous solution with 2*N*-hydrochloric acid. The bulky, white precipitate of the ester was taken up with ether and the extract rapidly dried and concentrated, when, on standing, most of the product separated in colourless nodules. The substance was recrystallised by addition of light petroleum to a benzene solution (at about 50°), the long, slender needles obtained having m. p. 125—126° (Found: C, 68·9; H, 5·8. $C_{20}H_{20}O_6$ requires C, 68·9; H, 5·7%). Ferric chloride added to an alcoholic solution developed a red coloration. When the ester (15 g.) was boiled with aqueous ammonia (10·8 c.c.; *d* 0·880) in water (100 c.c.) for 5 minutes, the chief products were benzamide and ethyl veratroylacetate; veratramide, veratric acid, and acetophenone were also formed. Benzoic acid and acetoveratrone did not appear to be among the products of hydrolysis.

2 : 4-*Dinitro*-3′ : 4′-*methylenedioxystilbene*.*—We have prepared

* This work on some derivatives of stilbene was carried out in collaboration with William Stafford.

some stilbene derivatives in order to attempt to obtain 2 : 6-naphthyridine derivatives by the dehydration of *oo*-diacylaminostilbenes.

A molten mixture of piperonal (23 g.), 2 : 4-dinitrotoluene (27 g.), and piperidine (30 drops) was heated on the steam-bath for 3 hours, when the mass became solid. The very sparingly soluble product crystallised from acetic acid in bright salmon prisms, m. p. 180° (Found : C, 57·3; H, 3·2. $C_{15}H_{10}O_6N_2$ requires C, 57·3; H, 3·2%).

4-*Nitro*-2-*amino*-3′ : 4′-*methylenedioxystilbene*.—A cooled solution of dinitromethylenedioxystilbene (20 g.) in acetic acid (300 c.c.) was mixed with a solution of crystallised stannous chloride (40 g.) in acetic acid containing hydrogen chloride and stirred in the cold for 6 hours. The orange-yellow tin salt obtained was digested with water, and from the free, red amino-derivative produced the hydrochloride was prepared in alcoholic solution, and decomposed by water. The base crystallised from alcohol in dark red prisms, m. p. 213° (Found : C, 63·3; H, 4·4. $C_{15}H_{12}O_4N_2$ requires C, 63·4; H, 4·2%). Its constitution may be inferred from the results of Thiele and Escales (*Ber.*, 1901, **34**, 2842) relating to the semi-reduction of 2 : 4-dinitrostilbene combined with the fact that ammonia and hydrogen sulphide reduced dinitromethylenedioxystilbene to a quite different isomeric base.

2 : 4-*Dinitro*-2′ : 3′-*dimethoxystilbene* was prepared from 2 : 4-dinitrotoluene (18 g.), 2 : 3-dimethoxybenzaldehyde (17 g.), and piperidine (20 drops) as described above. It crystallised from acetic acid in bright yellow prisms, m. p. 165° (yield 31 g.; 94%) (Found : C, 57·9; H, 4·4. $C_{16}H_{14}O_6N_2$ requires C, 58·2; H, 4·3%).

2-*Nitro*-4-*amino*-2′ : 3′-*dimethoxystilbene*.—The conditions for the satisfactory preparation of 2-nitro-4-aminostilbene itself have been studied and the following method gives good results (compare Thiele and Escales, *loc. cit.*). Hydrogen sulphide was led for 3 hours through a gently refluxing mixture of dinitrostilbene (20 g.), alcohol (250 c.c.), and aqueous ammonia (30 c.c.; *d* 0·880). The cooled solution was filtered, and the hydrochloride precipitated with hydrogen chloride; the base obtained from the salt separated from alcohol in red crystals, m. p. 110°.

Nitrostilbenediazonium hydrogen sulphate is readily isolable in the crystalline condition and on decomposition with aqueous potassium iodide gives 4-*iodo*-2-*nitrostilbene*, bright yellow crystals, m. p. 105°. A similar reduction process was applied to dinitro-2′ : 3′-dimethoxystilbene and orange-red needles, m. p. 121—122°, were obtained (Found : C, 63·6; H, 5·2. $C_{16}H_{16}O_4N_2$ requires C, 64·0; H, 5·3%).

2 : 4-*Dinitro*-3′ : 4′-*dimethoxystilbene*, prepared from veratraldehyde and 2 : 4-dinitrotoluene, crystallises from acetic acid in

stout, maroon prisms, m. p. 143°, sparingly soluble in alcohol (Found: C, 58·0; H, 4·4. $C_{18}H_{14}O_6N_2$ requires C, 58·2; H, 4·3%). When triturated with acetic acid (35 c.c.) and nitric acid (25 c.c.; *d* 1·42), the substance (19 g.) became yellow; the product crystallised from acetic acid in short, yellow prisms, m. p. 192° (Found: N, 11·3. $C_{16}H_{13}O_8N_3$ requires N, 11·2%).

2 : 4 : 6′-*Trinitro*-3′ : 4′-*dimethoxystilbene* is readily soluble in acetone, but sparingly soluble in most other organic solvents.

2 : 4-*Dinitro*-2′-*hydroxystilbene* is obtained in poor yield from 2 : 4-dinitrotoluene and salicylaldehyde in presence of piperidine. It crystallises from ethyl alcohol in light brown, irregular granules, m. p. 179—181° (Found: C, 58·6; H, 3·6. $C_{14}H_{10}O_5N_2$ requires C, 58·7; H, 3·5%), is readily soluble in most organic solvents, develops no coloration with alcoholic ferric chloride, and dissolves in aqueous sodium hydroxide to a red solution.

2 : 4-*Dinitro*-3′-*methoxy*-4′-*hydroxystilbene*, produced (yield 67%) by condensation of 2 : 4-dinitrotoluene and vanillin in presence of piperidine, crystallises from acetic acid in stout, vermilion prisms, m. p. 193° (Found: C, 57·0; H, 3·8. $C_{15}H_{12}O_6N_2$ requires C, 56·7; H, 3·9%).

We desire to thank the Carnegie Trust for the Universities of Scotland for a Scholarship which enabled one of us (J. M. G.) to take part in this investigation.

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CCI.—*The Rotatory Dispersive Power of Organic Compounds. Part XVII. β- and π-Sulphonic Derivatives of Camphor.*

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1. *Purpose of the Observations.*

THE experiments now described were undertaken in order to extend our knowledge of the rotatory dispersion of the derivatives of camphor, more particularly by including in the scope of our investigations a number of water-soluble compounds, since it appeared likely that the influence of the solvent would be reduced to a minimum when the optically active molecule is in a medium for which (just as in the case of a soap) it has no affinity except through the influence of a single ionisable group. Recent work on the orientation of the β-derivatives of camphor (this vol., p. 279)

has, however, made it possible also to draw important conclusions in reference to the influence of substitution on the dissymmetry of the camphor molecule in relation to its optical activity.

2. *Summary of Experimental Results.*

(a) *Abnormality of the π-Derivatives of Camphor.*—The data now recorded confirm the conclusion, already arrived at in the preceding paper (Part XVI) from the study of the halogen compounds, that there is something mysterious about the optical rotatory power of the π-derivatives of camphor. Thus, whereas the molecular rotatory powers of the α- and α′-bromo-derivatives of camphor and of β-bromocamphor differ by 425° and 540°, respectively (this vol., p. 1261), the corresponding derivatives of π-bromocamphor differ so little that the order of magnitude of their rotatory powers actually depends on the solvent chosen, the corresponding figure to those cited above being −47°. The present investigation has disclosed the further remarkable fact that, whilst the optical rotation of camphor, and of all the derivatives that have yet been examined (except camphorquinone), contains a high-frequency term (corresponding with the general absorption of a saturated molecule) and a low-frequency term (corresponding with the selective absorption of the unsaturated ketonic group), the rotatory power of many of the π-derivatives can be expressed, within the limits of experimental error, by a "simple" formula containing only a single low-frequency term. Thus the rotatory power of *ammonium α-bromocamphor-π-sulphonate*, $C_{10}H_{14}BrO\cdot SO_2\cdot ONH_4$ (Table I) in water agrees rigidly, over the whole range of the visual and photographic observations, with the theoretical values calculated from the "simple" dispersion equation $\alpha = 22{\cdot}015/(\lambda^2 - 0{\cdot}09668)$. The dispersion constant of this equation, $\lambda_0^2 = 0{\cdot}09668$ ($\lambda = 3109$ Å.U.), has the low frequency which is characteristic of the ketonic group, the high-frequency term of the parent ketone being reduced to such a small magnitude that it cannot be detected in the range of wave-lengths covered by the observations. The same behaviour was observed in *ammonium α-chlorocamphor-π-sulphonate*, $C_{10}H_{14}ClO\cdot SO_2\cdot ONH_4$ (Table II), the rotatory dispersion of which is also simple, and can be expressed completely, throughout the range covered by the visual and photographic observations, by the equation $\alpha = 17{\cdot}677/(\lambda^2 - 0{\cdot}09946)$, from which we can deduce the value $\lambda_0 = 3154$ Å.U. The photographic observations were less regular than in the case of the bromo-compound, but only because the settings of the analyser did not happen to correspond with strong lines in the iron spectrum.

In addition to these two salts, *α-bromocamphor-π-sulphonethyl-*

chloroamide,* $C_{10}H_{14}BrO{\cdot}SO_2{\cdot}NCl{\cdot}C_2H_5$ (Table III), and *α-bromocamphor-π-sulphondichloroamide*,* $C_{10}H_{14}BrO{\cdot}SO_2{\cdot}NCl_2$ (Table IV), gave a simple dispersion throughout the visible region (although in this case the curve was not followed into the photographic region), the value of the dispersion constant being $\lambda_0^2 = 0{\cdot}09969$ ($\lambda = 3157$ Å.U.) for the former and $\lambda_0^2 = 0{\cdot}10719$ ($\lambda_0 = 3200$) for the latter compound. An isomorphous mixture of the stereoisomeric *αα'-bromochlorocamphor-π-sulphonamides*,*

$$C_{10}H_{13}ClBrO{\cdot}SO_2{\cdot}NH_2,$$

the data for which are not reproduced, gave, however, a dispersion curve which, although it deviated only moderately from the simple law in the red, green, and blue regions, swung aside sharply in the violet, the dispersion being therefore obviously complex.

The predominance of the low-frequency term which is such a striking property of the π-sulphonic derivatives of camphor is not a completely new feature, since it can already be seen in the simple bromo-derivatives. Thus, whereas the two partial rotations of camphor are comparable in magnitude, the rotation constants of the low- and high-frequency terms being + 29·4 and — 20·1, respectively, the corresponding constants of απ-dibromocamphor are + 25·2 and — 5·7 only.

(b) *Properties of the* β-*Derivatives*.—Whereas the π-derivatives of camphor have an exceptionally high rotatory power, substitution in the β-position generally causes a diminution of rotatory power. Thus the rotatory power of Reychler's well-known camphorsulphonic acid, $C_{10}H_{14}O{\cdot}SO_2{\cdot}OH$ (Table V), in water, $[\alpha]_{5461} = +30{\cdot}4°$, $[M]_{5461} = +70{\cdot}7°$, is actually lower than that of camphor in benzene, $[\alpha]_{5461} = +52{\cdot}34°$, $[M]_{5461} = +79{\cdot}7°$ (compare β-bromocamphor, this vol., p. 1261). The dispersion of the acid is, however, obviously complex, since a simple formula which agrees with the data for the red and blue lines Zn 6362 and Zn 4811 shows a deviation of + 1·5° in the green, — 21° in the violet, and — 196° in the ultraviolet at 3969 Å.U. In this respect, the sulphonic acid closely resembles camphor itself; and it was found that by using the same dispersion constants as in the case of camphor (this vol., p. 612) a two-term formula could be fitted to the curve for the sulphonic acid with fairly good results, the maximum deviation in the photographic readings being about 2° in each case. Whereas, however, the deviations in the case of camphor were distributed irregularly as regards sign and magnitude, and were clearly within the limits of the errors of observation, the deviations in the case of the sulphonic acid (on readings of smaller magnitude) were obviously systematic, since the errors were all positive in the visual

* Available through the kindness of Prof. Pope and Mr. F. G. Mann.

region and all negative in the photographic region. A revised formula was therefore deduced in which the systematic errors were reduced to a small fraction of their former magnitude.* It should be noted that this was probably the only attempt that we have made to deduce the constants of a dispersion equation from external data, and that it was a failure, mainly because we were fortunate enough to be working with a long column of a strong aqueous solution of a transparent substance, so that our observed rotations were nearly twice as great as the specific rotations deduced from them.

As might be expected, the α-derivatives of Reychler's camphor-β-sulphonic acid show higher rotations than the parent compound. Thus potassium α-chlorocamphor-β-sulphonate, $C_{10}H_{14}ClO{\cdot}SO_2{\cdot}OK$ (Table VI), and potassium α-bromocamphor-β-sulphonate, $C_{10}H_{14}BrO{\cdot}SO_2{\cdot}OK$ (Table VII), gave *higher* rotations than camphor, namely, $[\alpha]_{5461} = +77{\cdot}4°$, $[M]_{5461} = +236°$ and $[\alpha]_{5461} = +111{\cdot}3°$, $[M]_{5461} = +389°$, respectively. The dispersions of these salts are complex but normal, the two partial rotations being of similar sign in each case.

The *sulphonamide*, $C_{10}H_{15}O{\cdot}SO_2{\cdot}NH_2$, of Reychler's acid is remarkable in being almost inactive, $[\alpha]_{5461} = +0{\cdot}4°$ only. It was therefore of interest to find out whether this small rotatory power was due to the small asymmetry of the compound, or to an anomalous dispersion, the small readings being then due merely to the observations falling in a region near to the wave-length at which an inversion of sign takes place. Observations for two other lines gave $[\alpha]_{5780} = -0{\cdot}8°$, $[\alpha]_{4358} = +15{\cdot}16°$, showing that there is actually a reversal of sign, although the rotations are still small, and do not indicate that any large optical rotatory power would be developed in the accessible region of the spectrum.

The *anhydramide*, $\begin{matrix} C_8H_{13}{-}CH_2 \\ | \quad\quad | \\ O_2S{-}N{=}C \end{matrix}$, of Reychler's acid (Table VIII) has a rotatory power, $[\alpha]_{5461} = -35{\cdot}9°$, $[M]_{5461} = -76{\cdot}5°$, of about the same magnitude as the parent compound, *but opposite in sign*, since the anhydramide derived from *d*-camphor is lævorotatory. The dispersion of this compound conforms closely to

* We are indebted to Mr. G. Owen, M.Sc., for this recalculation, which extended over a period of several months, and involved the investigation of more than a score of formulæ, before a satisfactory agreement was reached. The ultimate alteration in the constants was, however, relatively small, showing that a full series of readings fixes these constants within fairly narrow limits, thus :

	k_1.	k_2.	λ_1^2.	λ_2^2.
Old formula	21·523	−17·586	0·0872	0·0528
New formula	22·17	−18·32	0·085815	0·04945

Biot's law of inverse squares, but, on account of its small dispersion ratio, must be formulated as complex, just as in the analogous cases of sodium tartrate (Lowry and Austin, *Phil. Trans.*, 1922, *A*, **222**, 278) and octyl oxalate (Lowry and Richards, J., 1924, **125**, 1593). This observation is, however, of considerable interest in that, as a result of eliminating the ketonic double bond of camphor and replacing it by an imido-link in a closed ring, the *low-frequency term* in the dispersion equation has been reduced to a proportion which is almost negligible, whereas in the π-derivatives it is the *high-frequency term* which disappears from the equation.

3. *Relation between Rotatory Dispersion and Absorption.*

As in the case of Parts XV and XVI, publication of the dispersion data in the present paper has been delayed for more than a year in order to correlate them with measurements of absorption. A detailed comparison of the dispersion constants with the wave-lengths, λ_a, of the absorption bands now gives the results shown in the following table.

Dispersion Constants of Sulphonic Derivatives of Camphor.

	k_1.	k_2.	λ_1^2.	λ_2^2	λ_1.	λ_a.	$\lambda_1 - \lambda_a$.
Ammonium α-chlorocamphor-π-sulphonate	+17·677	—	0·09946	—	3150	3030	+120
Ammonium α-bromocamphor-π-sulphonate	+22·015	—	0·09668	—	3110	Am′ 3020 K′ 3040	+ 90
α-Bromocamphor-π-sulphonethylchloroamide	+25·889	—	0·09969	—	3160	—	—
α-Bromocamphor-π-sulphondichloroamide	+23·897	—	0·10719	—	3275	—	—
Camphor-β-sulphonic acid	+22·17	−18·32	0·08515	0·04945	2920	2850	+ 70
Camphor-β-sulphonanhydramide	—	−10·696	—	0*	—	—	—
Potassium α-chlorocamphor-β-sulphonate	+12·060	+ 5·1354	0·09768	—	3125	3000	+125
Potassium α-bromocamphor-β-sulphonate	+18·78	+ 5·569	0·09517	—	3085	3030	+ 55

* This compound conforms closely to Biot's law of rotatory dispersion.

In general, these constants follow one another fairly closely; thus Reychler's acid, which gives an abnormally small value for λ_1^2, is also seen to give an exceptionally small value for λ_a. As in all the cases hitherto examined, however, there is a steady discrepancy between the characteristic wave-lengths, λ_1 and λ_a,

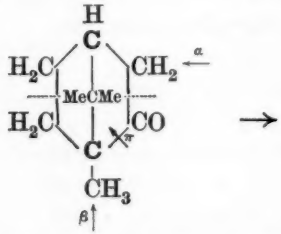
as deduced from the optical rotations and from the absorption spectra respectively. Since this discrepancy is in the same direction as in every previous case, and is, moreover, of the same order of magnitude, namely, 90 Å.U. as an average of five individual cases, it may now be regarded as a perfectly normal phenomenon. It therefore calls for no further comment, except to add that the "simple" one-term equations now worked out for some of the π-derivatives show just the same degree of concordance, and therefore rest on just as secure a foundation, as the "complex" two-term equations of the preceding paper of this series. In those cases, it was assumed in advance that the total rotation contains two partial rotations of unequal frequency; if a similar assumption were made in the present case, it would merely result in the development of equations in which $k_2 = 0$.

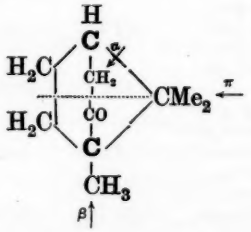
Attention may also be directed to the fact that camphor-β-sulphonanhydramide (in which the low-frequency partial rotation has disappeared from the equation as a sequel to eliminating the ketonic oxygen) is exceptionally transparent in the ultra-violet, and exhibits only a general absorption of light, without even a "step-out" to mark the presence of an incipient selective absorption (Lowry and Desch, J., 1909, **95**, 1343).

4. *Discussion of Experimental Results.*

In view of the proof that has recently been given (Wedekind, Schenk, and Stüsser, *Ber.*, 1923, **56**, 663; compare Lowry and Burgess, this vol., p. 279) that the β-derivatives, like the π-derivatives, are formed as a result of substitution in a methyl group, the three positions in which substitution can take place in the camphor molecule can be shown in two alternative aspects as in I and II :

(I.)





(II.)

Both methods of formulation bring out the fact that the molecule is almost symmetrical above and below the dotted horizontal line, and would indeed become completely symmetrical if (i) the >CO group were reduced to $>CH_2$, and (ii) the terminal methyl were replaced by hydrogen, or conversely. A still closer approach to symmetry can be seen in formula I, where the only element of

dissymmetry about a vertical plane perpendicular to that of the paper would again disappear if the CO group of camphor were reduced to CH_2.

(a) *Simple Dispersion of π-Derivatives.*—In summarising the experimental results it was stated that the rotatory dispersion of several of the π-derivatives can be expressed by means of a single term of Drude's equation, governed by a low-frequency dispersion constant only. In cases such as these, one may always suspect that the apparent simplicity of the low-frequency dispersion may mask the presence of a high-frequency term instead of eliminating it completely; but this does not excuse us from the necessity of inquiring why the high-frequency term has become impotent, or why this impotence should appear abruptly on passing from one group of compounds to another. The phenomenon to be accounted for is indeed very similar, whether the dispersion is fundamentally "simple" or only simple within the limits of experimental observation. In the analogous case of camphorquinone (J., 1924, **125**, 2511), the disappearance of the high-frequency term from the equation can be accounted for by noticing that (i) the low-frequency partial rotation of the unsaturated quinonoid group has a characteristic period in the visible spectrum, and therefore dominates completely the rotatory power of the molecule in the restricted region within which the compound is transparent, whilst (ii) the high-frequency partial rotation (which we attribute to the direct influence of the two asymmetric carbon atoms) is almost cancelled out by the growing symmetry of the molecule, since each asymmetric carbon atom is now adjacent to a CO group, and the only element of dissymmetry which remains is due to a contrast between hydrogen and methyl, so that *apo*camphorquinone (unlike *apo*camphor) would be optically inactive. In the case of the π-sulphonic derivatives these two asymmetric carbon atoms, which are already partly compensated in camphor itself, have been still more closely compensated by the introduction of symmetrically-placed sulphonic groups in the median plane between them, and therefore contribute only a negligible partial rotation to the total rotatory power of the molecule. In both cases, then, the disappearance of the high-frequency term can be associated with the approximate symmetry of the molecule about the median plane, just as in the case of camphoric anhydride, $C_8H_{14}\langle^{CO}_{CO}\rangle O$, the specific rotatory power of which is less than 1° (Lowry, J., 1903, **83**, 968).

(b) *Induced Asymmetry in the π-Derivatives of Camphor.*—The increased magnitude of the low-frequency partial rotations, which is such a striking property of the π-derivatives, can be accounted

for by noticing the increased difference between the groups on either side of the vertical plane in formula II, since it is this difference alone which makes it possible to attribute an "induced asymmetry" to the ketonic group. A much more striking anomaly is, however, to be found in the fact that the reversal of sign of the >CHBr group in the α- and α′-derivatives, which has an enormous effect on the rotatory power of camphor, produces an almost negligible change in the rotatory power of the π-derivatives. A clue to the explanation of this curious fact may be found in the suggestion, put forward more than 20 years ago, in order to explain the reactivity of the methyl group in π-sulphonation, namely, the possible "formation of a direct linkage between the ketonic carbon and a median methyl" (Armstrong and Lowry, J., 1902, **81**, 1473). A

TABLE I.

Rotations of Ammonium α-Bromocamphor-π-sulphonate in Water at 20°.

13·936 G. in 100 c.c. of solution.
Length of tube 6 dcm.

$[\alpha] = 1{\cdot}1959 \times \alpha.$
$[M] = 3{\cdot}2816 \times [\alpha].$

$$[\alpha] = \frac{22{\cdot}015}{\lambda^2 - 0{\cdot}09668}.$$

Visual readings.		[α] obs.	[α] calc.	[α] obs.—[α] calc.
Li	6708	+ 62·49°	+ 62·32°	+0·2°
Cd	6438	+ 69·09	+ 69·27	−0·2
Zn	6362	+ 71·28	+ 71·46	−0·2
Na	5893	+ 88·00	+ 87·91	+0·1
Cu	5782	+ 92·51	+ 92·64	−0·1
Hg	5780	+ 92·84	+ 92·73	+0·1
Cu	5700	+ 96·45	+ 96·45	±
Hg	5461	+109·40	+109·25	+0·2
Cu	5218	+125·35	+125·37	±
Cu	5153	+130·40	+130·37	±
Cu	5105	+134·35	+134·26	+0·1
Cd	5086	+135·93	+135·92	±
Zn	4811	+163·37	+163·41	±
Cd	4800	+164·67	+164·66	±
Zn	4722	+174·43	+174·31	+0·1
Zn	4680	+179·82	+179·93	−0·1
Cd	4678	+180·29	+180·21	+0·1
Hg	4358	+236·10	+236·06	±
Photographic readings.				
Fe	*4306*	*+248·1*	*+248·2*	*−0·1*
	4258	*+260·0*	*+260·1*	*−0·1*
	4213	*+272·0*	*+272·4*	*−0·4*
	4172	*+283·9*	*+284·5*	*−0·6*
	4135	*+295·9*	*+296·4*	*−0·5*
	4068	*+319·8*	*+319·9*	*−0·1*
	4010	*+343·7*	*+343·4*	*+0·3*

TABLE II.

Rotations of Ammonium α-Chlorocamphor-π-sulphonate in Water at 20°.

20·440 G. in 100 c.c. of solution.
Length of tube 6 dcm.

$[\alpha] = 0{\cdot}81540 \times \alpha.$
$[M] = 2{\cdot}8370 \times [\alpha].$

$$[\alpha] = \frac{17{\cdot}677}{\lambda^2 - 0{\cdot}09946}.$$

		[α] obs.	[α] calc.	[α] obs.—[α] calc.
		+ 50·37°	+ 50·44°	−0·07°
		+ 56·03	+ 56·10	−0·07
		+ 57·89	+ 57·89	±
		+ 71·32	+ 71·38	−0·06
		+ 75·25	+ 75·26	−0·01
		+ 75·34	+ 75·34	±
		+ 78·39	+ 78·40	−0·01
		+ 88·97	+ 88·95	+0·02
		+102·32	+102·28	+0·04
		+106·53	+106·42	+0·11
		+109·60	+109·65	−0·05
		+111·10	+111·04	+0·06
		+133·96	+133·96	±
		+134·90	+135·01	−0·11
		+142·94	+143·10	−0·16
		+147·77	+147·83	−0·06
		+148·06	+148·06	±
		+194·70	+195·35	−0·65
Fe	*4315*	*+202·9*	*+203·8*	*−0·9*
	4277	*+211·0*	*+211·8*	*−0·8*
	4239	*+219·2*	*+220·3*	*−1·1*
	4204	*+227·3*	*+228·7*	*−1·4*
	4171	*+235·5*	*+237·3*	*−1·8*
	4150	*+243·6*	*+242·9*	*+0·7*
	4055	*+268·1*	*+265·9*	*+2·2*

TABLE III.

Rotations of α-Bromocamphor-π-sulphonethylchloroamide in Chloroform at 20°.

14·287 G. in 100 c.c. of solution. Length of tube 2 dcm.

$[\alpha] = 3{\cdot}4997 \times \alpha.$ $[M] = 3{\cdot}7264 \times [\alpha].$

$$[\alpha] = \frac{25{\cdot}889}{\lambda^2 - 0{\cdot}09969}.$$

Visual readings.		[α] obs.	[α] calc.	[α] obs.−[α] calc.
Li	6708	+ 73·9°	+ 73·9°	±
Cd	6438	+ 82·3	+ 82·2	+0·1°
Zn	6362	+ 84·9	+ 84·9	±
Na	5893	+104·3	+104·6	−0·3
Cu	5782	+110·2	+110·3	−0·1
Hg	5780	+110·5	+110·5	±
Cu	5700	+114·4	+114·9	−0·5
Hg	5461	+130·4	+130·4	±
Cu	5218	+150·0	+150·0	±
Cu	5153	+156·0	+156·1	−0·1
Cu	5105	+160·6	+160·8	−0·2
Cd	5086	+162·8	+162·8	±
Zn	4811	+196·7	+196·5	+0·2
Cd	4800	+196·9	+198·0	−1·1
Zn	4722	+210·5	+210·0	+0·5
Zn	4680	—	—	—
Cd	4678	+217·3	+217·3	±
Hg	4358	+286·5	+286·8	−0·3

TABLE IV.

Rotations of α-Bromocamphor-π-sulphondichloroamide in Chloroform at 20°.

10·8716 G. in 100 c.c. of solution. Length of tube 2 dcm.

$[\alpha] = 4{\cdot}5992 \times \alpha.$ $[M] = 3{\cdot}7905 \times [\alpha].$

$$[\alpha] = \frac{23{\cdot}897}{\lambda^2 - 0{\cdot}10719}.$$

Visual readings.		[α] obs.	[α] calc.	[α] obs.−[α] calc.
Li	6708	+ 69·7°	+ 69·7°	±
Cd	6438	+ 78·1	+ 77·8	+0·2°
Zn	6362	+ 80·9	+ 80·3	+0·6
Na	5893	+ 99·0	+ 99·6	−0·6
Cu	5782	+106·3	+105·2	+0·8
Hg	5780	+105·1	+105·3	−0·2
Cu	5700	+109·7	+109·8	−0·1
Hg	5461	+125·0	+125·1	−0·1
Cu	5218	+145·3	+144·7	+0·6
Cu	5153	+151·2	+150·9	+0·3
Cu	5105	+155·8	+155·7	+0·1
Cd	5086	+158·1	+157·8	+0·3
Zn	4811	+192·4	+192·4	±
Cd	4800	+194·5	+194·0	+0·5
Zn	4722	+205·7	+206·4	−0·7
Zn	4680	+213·4	+213·7	−0·3
Cd	4678	+215·0	+214·0	+1·0
Hg	4358	+286·0	+288·8	−2·8

TABLE V.

Rotations of Camphor-β-sulphonic Acid in Water at 20°.

28·636 G. in 100 c.c. of solution. Length of tube 6 dcm.

$[\alpha] = 0{\cdot}58202 \times \alpha.$ $[M] = 2{\cdot}3222 \times [\alpha].$

$$[\alpha] = \frac{22{\cdot}17}{\lambda^2 - 0{\cdot}08515} - \frac{18{\cdot}32}{\lambda^2 - 0{\cdot}04945}.$$

Visual readings.		[α] obs.	[α] calc.	[α] obs.−[α] calc.	Photographic readings.	[α] obs.	[α] calc.	[α] obs.−[α] calc.
Li	6707·85	+15·05°	15·03°	+0·02°	*Fe 4299*	*+ 87·06°*	*87·11°*	*−0·05°*
Cd	6438·47	+17·13	17·11	+0·02	*4246*	*+ 92·88*	*93·02*	*−0·14*
Zn	6362·35	+17·81	17·80	+0·01	*4192*	*+ 98·70*	*99·69*	*−0·99*
Na	5892·95	+23·11	23·11	±	*4155*	*+104·52*	*104·69*	*−0·17*
Cu	5782·16	+24·68	24·66	+0·02	*4114*	*+110·34*	*110·69*	*−0·35*
Hg	5780·13	+24·68	24·69	−0·01	*4078*	*+116·16*	*116·42*	*−0·26*
Cu	5700·25	+25·93	25·96	−0·03	*4041*	*+121·98*	*122·69*	*−0·71*
Hg	5460·74	+30·44	30·41	+0·03	*4014*	*+127·80*	*127·77*	*+0·03*
Cu	5218·70	+36·35	36·41	+0·06	*3982*	*+133·62*	*134·09*	*−0·47*
Cu	5153·25	+38·20	38·12	−0·08	*3969*	*+136·8*	*136·79*	*+0·01*
Cu	5105·54	+39·57	39·57	±				
Cd	5085·82	+40·25	40·21	+0·04				
Zn	4810·54	+51·07	50·90	+0·17				
Cd	4799·92	+51·61	51·39	+0·22				
Zn	4722·16	+55·46	55·33	+0·13				
Zn	4680·14	+57·65	57·60	+0·05				
Cd	4678·16	+57·84	57·68	+0·16				
Hg	4358·34	+81·24	81·15	+0·09				

TABLE VI.

Rotations of Potassium α-Chloro-camphor-β-sulphonate in Water at 20°.

12·386 G. in 100 c.c. of solution.
Length of tube 6 dcm.

$[a] = 1{\cdot}3456 \times a.$
$[M] = 3{\cdot}0476 \times [a].$

$$[a] = \frac{12{\cdot}060}{\lambda^2 - 0{\cdot}09768} + \frac{5{\cdot}1354}{\lambda^2}.$$

	Visual readings.	[a] obs.	[a] calc.	[a] obs.−[a] calc.
Li	6707·85	+ 45·75°	+ 45·65°	+0·10°
Cd	6438·47	+ 50·42	+ 50·45	−0·03
Zn	6362·35	+ 51·95	+ 51·95	±
Na	5892·95	+ 63·03	+ 63·16	−0·13
Cu	5782·16	+ 66·28	+ 66·32	−0·04
Hg	5780·13	+ 66·42	+ 66·38	+0·04
Cu	5700·25	+ 68·94	+ 68·88	+0·06
Hg	5460·74	+ 77·43	+ 77·37	+0·06
Cu	5218·70	+ 87·97	+ 87·93	+0·04
Cu	5153·25	+ 91·21	+ 91·18	+0·03
Cu	5105·54	+ 93·72	+ 93·71	+0·01
Cd	5085·82	+ 94·76	+ 94·77	−0·01
Zn	4810·54	+112·78	+112·37	+0·41
Cd	4799·92	+113·45	+113·15	+0·30
Zn	4722·16	+119·55	+119·35	+0·20
Zn	4680·14	+123·23	+122·72	+0·51
Cd	4678·16	+123·43	+122·99	+0·44
Hg	4358·34	+158·24	+157·74	+0·50
	Photographic readings.			
Fe	*4359*	*+158·24*	*+157·65*	*+0·59*
	4268	*+171·70*	*+170·95*	*+0·75*
	4185	*+185·15*	*+185·01*	*+0·14*
	4113	*+198·61*	*+199·05*	*−0·44*
	4055	*+212·07*	*+211·91*	*+0·16*
	3952	*+238·98*	*+239·02*	*−0·04**

TABLE VII.

Rotations of Potassium α-Bromo-camphor-β-sulphonate in Water at 20°.

16·206 G. in 100 c.c. of solution.
Length of tube 6 dcm.

$[a] = 1{\cdot}0284 \times a.$
$[M] = 3{\cdot}4922 \times [a].$

$$[a] = \frac{18{\cdot}78}{\lambda^2 - 0{\cdot}09517} + \frac{5{\cdot}569}{\lambda^2}.$$

	[a] obs.	[a] calc.	[a] obs.−[a] calc.
	—	—	—
	+ 72·26°	+ 72·36°	−0·10°
	+ 74·43	+ 74·43	±
	+ 90·60	+ 90·61	−0·01
	+ 94·25	+ 94·20	+0·05
	+ 95·38	+ 95·30	+0·08
	+ 99·05	+ 98·90	+0·15
	+111·32	+111·20	+0·12
	+126·26	+126·50	−0·24
	+130·16	+131·16	−1·00
	+134·40	+134·85	−0·45
	+136·38	+136·10	+0·28
	+161·84	+161·93	−0·09
	+162·99	+163·07	−0·08
	+171·95	+171·92	+0·03
	—	—	—
	+177·24	+177·31	−0·07
	+227·35	+227·46	−0·11
Fe	*4306*	*+237·64*	*+238·14*	*−0·50*
	4260	*+247·92*	*+248·29*	*−0·37*
	4176	*+268·49*	*+269·25*	*−0·76*
	4101	*+289·06*	*+290·29*	*−0·23*
	4071	*+299·34*	*+299·75*	*−0·41*
	4041	*+309·63*	*+309·74*	*−0·11†*

* Deviation from simple formula $[a] = 16{\cdot}699/(\lambda^2 - 0{\cdot}08335)$, obs. − calc. = + 10·0°.

† Deviation from simple formula $[a] = 23{\cdot}891/(\lambda^2 - 0{\cdot}08379)$, obs. − calc. = + 9·1°.

Note.—The dispersion formulæ for these two compounds, which have been calculated by Mr. G. Owen, M.Sc., contain two partial rotations of similar sign, and therefore provide two more examples of the type of complex rotatory dispersion which has been described as "impossible to detect in practice" (compare footnote, this vol., p. 1262). The deviations from the simple formulæ (calculated to fit the red and blue zinc lines) are, however, already substantial even in the intermediate green region of the spectrum, and increase to about 2° in the case of the mercury violet line, and to about 10° at the extreme end of the visible spectrum; they are therefore far too obvious to be overlooked. This type of rotatory dispersion, although quite easy to detect in this series of compounds, is not common, since the induced asymmetry of the ketonic group is always opposite in sign to the fixed asymmetry of the camphor nucleus, except when the sign of the latter has been reversed by the creation of a new positive partial rotation as a result of introducing a substituent in the *a*-position.

TABLE VIII.

Rotations of Camphor-β-sulphonanhydramide in Acetone at 20°.

4·941 G. in 100 c.c. of solution. Length of tube 6 dcm.

$[\alpha] = 3{\cdot}3731 \times \alpha$. $[M] = 2{\cdot}1322 \times [\alpha]$. $[\alpha] = -10{\cdot}696/\lambda^2$.

Visual readings.		[α] obs.	[α] calc.	[α] obs.— [α] calc.	Visual readings.		[α] obs.	[α] calc.	[α] obs.— [α] calc.
Li	6708	−23·5°	−23·8°	+0·3°	Cu	5105	−41·0°	−41·0°	±
Cd	6438	−25·7	−25·8	+0·1	Cd	5086	−41·5	−41·4	−0·1°
Zn	6362	−26·4	−26·4	±	Zn	4811	−46·2	−46·2	±
Na	5893	−30·9	−30·8	−0·1	Zn	4722	−47·6	−48·0	+0·4
Cu	5782	−31·9	−32·0	+0·1	Cd	4678	−49·2	−48·9	−0·3
Hg	5780	−32·1	−32·0	−0·1	Hg	4358	−56·1	−56·3	+0·2
Cu	5700	−33·1	−32·9	−0·2	Photographic readings.				
Hg	5461	−35·9	−35·9	±	*Fe*	*4299*	*−57·8*	*−57·9*	*+0·1*
Cu	5218	−39·3	−39·3	±		*4220*	*−59·4*	*−60·1*	*+0·6*
Cu	5153	−40·6	−40·3	−0·3					

formula was then given which shows the formation of a new ring by the transference of a hydrogen atom from the π-methyl group to the ketonic oxygen; but it would be more in accord with our present views to postulate only a co-ordination of the reactive π-hydrogen atom with the ketonic oxygen. This co-ordination would have the advantage of enabling us to attribute the induced asymmetry of the ketonic group to a more concrete influence than that of a mere unsymmetrical field of force. It would, moreover, permit of a very simple explanation of the fact that the partial rotation of the ketonic group is always positive in sign, and is not even altered substantially in magnitude when the specific rotation of the molecule is shifted through several hundred degrees by reversing the sign of the >CHBr radical which is immediately adjacent to the ketonic group. In the π-derivatives this particular type of co-ordination is prevented by the elimination of the π-hydrogen atom; the two adjacent groups are therefore free to adjust themselves in such a way that a reversal of the fixed asymmetry of the saturated >CHBr group at once produces a compensating change in the induced asymmetry of the unsaturated >C=O group, whereby the balance of the molecule as expressed by its optical rotatory power is preserved almost unchanged.

5. *Summary.*

(*a*) The rotatory dispersion and absorption spectra of a series of β- and π-sulphonic derivatives of camphor have been determined. As in previous cases, there is a discrepancy of nearly 100 Å.U. between the characteristic frequencies deduced from the two series of observations.

(*b*) The rotatory dispersion of several of the π-derivatives can be expressed by one term of Drude's equation, the high-frequency

partial rotation being negligible in comparison with the magnitude of the low-frequency term, just as in the case of camphorquinone.

(*c*) The β-derivatives all exhibit complex dispersion, but the anhydramide nearly obeys Biot's law, since the low-frequency partial rotation and the band of selective absorption both disappear as a sequel to the elimination of the ketonic oxygen.

We are indebted to the Department of Scientific and Industrial Research for a maintenance grant to one of us (E. M. R.) during the period in which this research was carried out. We are also indebted to Prof. Pope and Mr. F. G. Mann for the loan of some of the compounds examined.

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CCII.—*Sulphur Sesquioxide.*

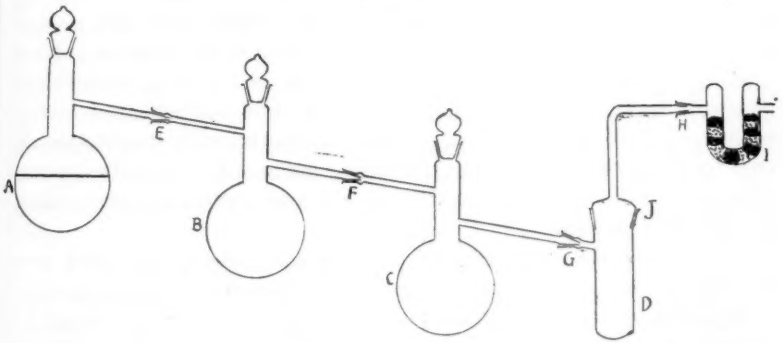
By ISRAEL VOGEL and JAMES RIDDICK PARTINGTON.

FROM the reaction between sulphur and sulphur trioxide Vogel (*J. Chem. Phys.*, 1812, **4**, 121) isolated a deep blue liquid, a bluish-green solid, and a brown liquid, all of which were considered to be definite compounds of sulphuric anhydride and sulphur. Similar results were obtained by Schweigger (*ibid.*, 1815, **13**, 484). Wach (*ibid.*, 1827, **50**, 1) endeavoured to determine the composition of the blue, green, and brown substances and found that the amount of sulphur combined with a definite quantity of sulphur trioxide increased in the order named. Fischer (*Ann. Phys. Chem.*, 1829, **16**, 119) and Rose (*ibid.*, 1834, **32**, 98) considered that the blue liquid contained a definite compound, whilst Berzelius ("Traité de Chimie," 1845, Tome I, p. 459) maintained that no new oxide of sulphur was present, and Stein (*J. pr. Chem.*, 1873, **6**, 172) ascribed the colour of the solution to the presence of finely divided sulphur. Weber (*Ann. Phys. Chem.*, 1875, **156**, 531) found the sulphur content of the bluish-green solid to correspond with S_2O_3. No further work appears to have been done, and the current view seems to be that the supposed sulphur sesquioxide is a "colloidal solution" (compare Hofmann, "Anorganische Chemie," 1920, p. 166; Ephraim, "Anorganische Chemie," 1922, p. 437). The present research was accordingly undertaken with the object of definitely deciding between these two theories and of studying the properties of the substance if it were proved to be a chemical compound.

The starting materials of previous investigators were far from pure, and this was probably the cause of the different results obtained.

Purification of Sulphur.—The purest commercial precipitated sulphur was distilled in a Pyrex retort in a current of pure carbon dioxide, the distillate being collected and allowed to solidify in a Jena glass flask; the first and last fractions were neglected. The distillate was melted and the liquid poured on to watch-glasses of Jena glass, the melting and cooling being conducted in an atmosphere of dry carbon dioxide. When the sulphur had almost completely resolidified, it was cut up into small pieces and the above process repeated three times, considerable head and tail fractions being discarded in each distillation. After the first distillation, the sulphur did not darken appreciably but melted to a clear and mobile liquid which, with rise of temperature, exhibited all the usual phenomena, but did not darken appreciably. The purified sulphur

FIG. 1.



was finely powdered and preserved in a vacuum desiccator over phosphorus pentoxide until required.

Preparation of Pure Sulphur Trioxide.—Although many types of apparatus have been devised and employed for the preparation of pure sulphur trioxide (compare Weber, *Ann. Phys. Chem.*, **1876**, **159**, 313; Divers and Shimosé, *Ber.*, 1883, **16**, 1009; Schenk, *Annalen*, 1901, **316**, 1; Lichty, *J. Amer. Chem. Soc.*, 1908, **30**, 1834; Beckmann, *Z. anorg. Chem.*, 1912, **77**, 90), none of these permit of the preparation of large quantities of the anhydride in a comparatively short time, nor do they allow of the convenient handling of the pure product. The apparatus shown in Fig. 1 was constructed for the preparation of pure sulphuric anhydride from oleum. The apparatus was entirely of Durosil resistance glass. The three distilling flasks, A, B and C, and a reaction vessel D were connected by interchangeable ground joints. Stoppers were ground to fit the mouths of the flasks and reaction vessel and also both parts of the joints E, F and G so that any flask or flasks could be

removed from the remainder of the apparatus without access of moisture. A phosphorus pentoxide drying tube, I, was attached to the reaction vessel by means of the joint H.

Kahlbaum's pure 65% oleum (about 200 c.c.) was placed in A, B was immersed in a bath of ice-cold water, C surrounded by a freezing mixture of finely-ground ice, and the bath of concentrated sulphuric acid surrounding A was very carefully warmed. Sulphur trioxide distilled over and condensed in B, only a very small quantity finding its way to C. The sulphuric anhydride which passed over on gentle heating was the only portion collected. After distillation and some cooling, the flask A was detached at E and immediately replaced by a ground glass stopper. B was then placed in the sulphuric acid bath, C surrounded by cold water, D immersed in a freezing mixture of ice and salt, and the bath surrounding B very gently warmed. Sulphur trioxide distilled into C, the distillation being stopped when about three-quarters of the contents of B had passed over: flask B was then removed and replaced by a ground glass stopper. Flasks B and A after cleaning and drying were then attached to the apparatus and the distillation was repeated in the manner described. In this way, pure sulphur trioxide was obtained, two to three distillations usually being sufficient. It melted completely at about 15° to a colourless liquid and crystallised on cooling in beautiful needles.

To transfer the anhydride to the reaction vessel, the solid was melted and the flasks were rotated about the ground glass joints.

Preparation and Analysis of Sulphur Sesquioxide.—A mode of procedure similar to that described by Weber (*Ann. Chem. Phys.*, 1875, **156**, 531) was first employed. About 20 c.c. of liquid sulphuric anhydride were placed in the reaction vessel and the latter was closed by a ground glass stopper at G. Sulphur was then added in small quantities by momentarily detaching the ground glass joint J, a fresh portion being added only after the previous quantity had entered into combination. The sulphur on coming in contact with the anhydride formed blue drops, most of which sank, but some became attached to the sides of the vessel near the surface of the sulphur trioxide. In order to avoid formation of a cake of solid at the surface, the vessel must be shaken during the preparation, when most of the substance sinks as soon as formed. If the sulphur be added too rapidly, the temperature of the sulphuric anhydride rises and the solid near the surface decomposes with the evolution of sulphur dioxide. If, however, the vessel be shaken during the addition and care be taken that the temperature does not rise above 15°, very little decomposition occurs. After about 1 or 2 g. of sulphur had been added, the excess of liquid sulphur trioxide,

which should be colourless, was poured off and any still remaining removed by warming in a vacuum at 30—40°, two towers, containing concentrated sulphuric acid on pumice and borax on glass wool respectively, being interposed before the pump. All the sulphuric anhydride could not be easily removed in this manner and it was necessary first to powder the bluish-green substance in an atmosphere of dry carbon dioxide and then to heat in a vacuum as described. Weber's compound probably contained small quantities of occluded sulphur trioxide, since he attempted to remove the latter merely by warming to " blood " temperature.

The substance thus obtained was a bluish-green solid, which soon decomposed at the ordinary temperature with the evolution of sulphur dioxide, sulphur remaining. Decomposition was accelerated by warming. The compound was very hygroscopic; if left exposed to the air, decomposition occurred and moist sulphur remained. If all the sulphuric anhydride had been removed, the substance was stable for several minutes at about 15°. In carrying out the analyses the weighings were performed as rapidly as possible.

Weber's method of analysis (*loc. cit.*) was first repeated and confirmed. Some of the substance was weighed out into a small glass-stoppered tube and, after removing the stopper, the tube was allowed to slide down the side of another but larger glass-stoppered vessel containing a mixture of concentrated and fuming nitric acids, great care being taken that the acid did not reach the contents of the small tube. The larger tube was then stoppered and completely wrapped in a cloth, since explosions sometimes resulted. The vessel was inclined so that the acid came in contact with the substance; a violent reaction ensued, and the stopper was held down. The whole was allowed to stand over-night. The contents of the tube were then diluted and the precipitated sulphur was collected on a weighed Gooch crucible. The sulphur in the filtrate was estimated, after the nitric acid had been boiled off, with barium chloride solution in the usual manner. The results are given in Table I.

TABLE I.

G. of substance.	G. of precipitated S.	G. of $BaSO_4$-S.	Total percentage of S.
0·4272	0·1074	0·1365	57·09
0·5870	0·1484	0·1876	57·24
0·5106	0·1202	0·1722	57·27
		Calculated for S_2O_3	57·19

In another method of analysis the sulphur of the compound was oxidised to sulphuric acid in one operation by a mixture of fuming nitric acid and bromine, the operation being carried out in the manner described. Of some twenty-five analyses carried out by this method, four exploded. A few typical results are

recorded in Table II : all the successful analyses were between the limits of 56·96 and 57·81% sulphur.

TABLE II.

G. of substance.	G. of $BaSO_4$.	G. of S.	Total percentage of S.
0·2103	0·8775	0·1206	57·32
0·5105	2·1671	0·2977	57·31
0·3030	1·2605	0·1732	57·15
0·4900	2·0356	0·2797	57·08
0·1696	0·7055	0·0969	57·15
		Calculated for S_2O_3	57·19

The results are in agreement with those found by the first method and with the value required by S_2O_3. It appears, therefore, that the substance has a constant chemical composition.

The method of preparation of the compound given above is somewhat laborious and cannot be used for the preparation of comparatively large quantities. It was found that instead of adding the sulphur to the liquid sulphuric anhydride, one might add the latter to the former and obtain a similar result. About 1 g. of finely-powdered sulphur was placed in the reaction vessel and about 15 c.c. of liquid sulphur trioxide were added. No reaction appeared to take place at first, although the whole assumed a deep blue colour and became somewhat viscid. After approximately 30 seconds, a violent reaction set in, so that it was found advisable to detach the phosphorus pentoxide tube from the reaction vessel, clouds of white fumes being evolved. After about 2 minutes the reaction subsided, the supernatant liquid sulphuric anhydride, which was coloured very pale blue, was poured off, and the residual sulphur trioxide removed from the resultant bluish-green solid in the manner already described. The bluish-green solid * thus obtained dissolved in oleum with the production of a deep blue solution, decomposed on exposure to air and on keeping with the evolution of sulphur dioxide, absorbed moisture from the air, and appeared to be identical with the substance prepared by the first method. The analysis by the fuming nitric acid and bromine method yielded the following results :

TABLE III.

G. of substance.	G. of $BaSO_4$.	G. of S.	Total percentage of S.
0·1994	0·8296	0·1140	57·16
0·2316	0·9660	0·1327	57·30
0·1778	0·7406	0·1017	57·22
		Calculated for S_2O_3	57·19

This method of preparation is simpler and more convenient than the first one, and the residual sulphuric anhydride from one preparation

* On some occasions the solid was green.

may be employed again for the conversion of another quantity of sulphur into the sesquioxide.

Owing to the great instability of the compound a number of experiments were performed with a view to render it more stable. It was found that the solid could be kept unchanged for several hours in a completely dry oxygen-free atmosphere at low pressures (less than 1 mm. of mercury). Cooling to liquid air temperatures had no appreciable effect.

The empirical formula of the compound has been shown to be $(S_2O_3)_x$, which for the sake of simplicity was taken as S_2O_3. From this it would seem that the substance might be the anhydride of hyposulphurous acid, but it may be said at once that all attempts to convert it into either the acid or its simple derivatives failed, owing to the simultaneous side and consecutive reactions and the production of mixtures of complicated sulphuroxy-acids, the reactions and identification of which are described below.

It was thought that the formula of the compound might be established by processes similar to those employed by Bernsthen (*Annalen*, 1881, **208**, 142) for sodium hyposulphite, but it was found that substances are formed in solution which complicate the reactions and that no evidence as to the constitution of the substance can be obtained from these results.

The molecular weight of the substance was not determined, since no solvent could be found with which the compound did not react. Purified phosphorus oxychloride, the only pure solvent for sulphuric anhydride at present known (compare Lichty, *J. Amer. Chem. Soc.*, 1912, **34**, 1441), caused complete decomposition of the sulphur sesquioxide.

Owing to the extremely reactive and unstable nature of the substance, all attempts to deduce its constitution by methods usually applicable to acid anhydrides were unsuccessful. Nevertheless, the results obtained could be completely reconciled with the formula S_2O_3 for the original compound.

Properties of Sulphur Sesquioxide.—Sulphur sesquioxide dissolves in oleum with the formation of a deep blue solution identical with that produced by the addition of sulphur. A solution of indigo in concentrated sulphuric acid or of indigo-carmine in water is partially decolorised; in no case could complete decoloration be effected even by the addition of comparatively large quantities of the substance. A similar reaction takes place with strongly ammoniacal copper sulphate solution, the decoloration being only partial.

With anhydrous ether a violent reaction takes place, the compound decomposing with the separation of sulphur and the production of a yellow solution; on decanting the clear, evil-smelling

liquid and distilling off the ether, a very small quantity of a yellow oil remained. The amount, however, was too small for analysis and qualitative tests pointed to the presence of sulphur.

A similar reaction takes place with absolute (100%) ethyl alcohol. Here a very small quantity of a pale yellow liquid was obtained after removal of the separated sulphur by filtration and the alcohol by distillation. The amount was too small for analysis, but qualitative tests indicated the presence of sulphur.

Sulphur sesquioxide when allowed to come into contact with water decomposes, a pale yellow solution (compare hyposulphurous acid) being momentarily formed, the decomposition being accompanied by a loud hissing noise and the simultaneous formation of a milky solution due to the separation of sulphur. If a relatively large quantity of the sesquioxide be employed, yellow sulphur separates, which when freshly formed is somewhat plastic, but soon becomes brittle. The filtered solution contained sulphuric acid and trithionic acid, together with small quantities of penta- and possibly tetra-thionic acids, as detected by the reactions with mercurous nitrate, cupric sulphate, mercuric chloride, and ammoniacal silver nitrate solutions, respectively (compare Takamatsu and Smith, J., 1880, **37**, 592; Debus, J., 1888, **53**, 278; Riesenfeld and Feld, *Z. anorg. Chem.*, 1921, **119**, 225; Forster and Hornig, *ibid.*, 1922, **125**, 86), whilst the presence of sulphurous acid was indicated by the coloration with ferric chloride solution. The yellow coloration with ferric chloride solution is not, however, exclusive to sulphurous acid (compare Debus, *loc. cit.*), but is also produced by sulphoxylic acid and its salts (*vide infra*), hence both these substances may have been present. That the yellow coloration is due to a substance other than sulphurous acid is probable, since after removing the latter by the passage of a current of air through the solution for several hours, the residual liquid gave a yellow coloration with ferric chloride. The complete removal of sulphur dioxide was detected by inserting two flasks, the first containing a known volume of standard iodine solution and the second a known volume of standard thiosulphate solution, before the pump, and titrating: the total quantity of iodine remained unaltered when the process was complete. The quantities of tetra- and pentathionic acids increased with time, as was shown by the yellow opalescence produced on the addition of the first few drops of mercurous nitrate solution. No qualitative tests are at present known by which small quantities of tetrathionic acid or its salts may be detected in the presence of pentathionic acid or its salts, hence the conclusion as to the presence of tetrathionic acid in the solution is somewhat doubtful.

The initial reaction with water may consist in the decomposition of the sulphur sesquioxide into monoxide and dioxide :

$$S_2O_3 = SO + SO_2.$$

Some of the monoxide polymerises, the polymeride in the presence of water forming pentathionic acid :

$$5SO + H_2O = H_2S_5O_6$$

(compare Debus, *loc. cit.*; Riesenfeld and Feld, *loc. cit.*), whilst another portion reacts with water to produce sulphoxylic acid :

$$SO + H_2O = H_2SO_2.$$

The chief reaction, however, consists in the formation of trithionic acid; two modes of interaction are possible, the first being between water, sulphur sesquioxide and sulphur dioxide :

$$S_2O_3 + SO_2 + H_2O = H_2S_3O_6,$$

and the second between sulphur monoxide, sulphur dioxide and water :

$$SO + 2SO_2 + H_2O = H_2S_3O_6.$$

The latter reaction probably take place to the greater extent. If the solution be kept for some time, the trithionic acid gradually combines with *nascent* sulphur with the production of tetra- and penta-thionic acids :

$$H_2S_3O_6 + S = H_2S_4O_6;$$
$$H_2S_4O_6 + S = H_2S_5O_6;$$
$$H_2S_3O_6 + 2S = H_2S_5O_6.$$

The last reaction to be studied was that with an anhydrous alcoholic solution of sodium ethoxide, prepared by adding sodium to absolute ethyl alcohol in a Jena flask fitted with a reflux condenser and phosphorus pentoxide drying tube. On addition of sulphur sesquioxide, an extremely vigorous reaction took place, small quantities of a yellow, crystalline solid separating out and the whole liquid assuming a yellowish-brown colour. The product of the reaction had a very strong and unpleasant odour somewhat resembling that of garlic and affecting the voice if the vapour was inhaled for any length of time. On adding sulphuric acid immediately after the reaction a white solid was precipitated, which was separated by adding absolute alcohol, filtering, and drying over phosphorus pentoxide. The solid was fairly soluble in water, neither the solution nor the solid decolorising indigo or ammoniacal cupric sulphate solutions. Qualitative tests indicated the presence of sulphur and sodium. The sodium was determined as sulphate,

whilst the sulphur was estimated by fusion with a mixture of sodium peroxide and sodium carbonate (Treadwell-Hall, "Quantitative Analysis," 1919, p. 849) and in a second process by oxidation with a mixture of fuming nitric acid and bromine, as detailed above. The latter method is much more convenient than the first. The results of the analyses agreed fairly well with those required by *sodium ethyl sulphoxylate* (Found: Na, 20·10, 20·06; S, 27·80, 27·85. $NaEtSO_2$ requires Na, 19·81; S, 27·61%).

Unless extreme precautions are taken to prevent the access of moisture, and unless the substance is isolated immediately after the reaction, the resulting solid consists of a mixture of sodium ethyl sulphoxylate and its hydrolysis product. The completely hydrolysed product was isolated from the solution by allowing it to stand over-night and then gradually acidifying with dilute sulphuric acid; a yellow precipitate separated which became white as soon as the whole solution was acid. The precipitate was immediately filtered with the aid of the pump, washed with absolute alcohol, and dried over phosphorus pentoxide for a week. A perfectly white, crystalline solid was obtained which remained unchanged when heated at 110° for 2 hours. The sulphur content was determined by the fuming nitric acid and bromine method; in the estimation of sodium the substance was first decomposed with a boiling mixture of fuming nitric acid and bromine, evaporated to small bulk, diluted with water, and transferred to a weighed platinum dish, the estimation for sodium as sulphate being continued in the usual manner (Found: Na,40·24, 41·08, 41·04; S, 29·16, 29·20, 29·14. Na_2SO_2 requires Na, 41·80; S, 29·13%).

Sodium sulphoxylate is moderately soluble in cold and more soluble in hot water and sparingly soluble in alcohol. It is practically unattacked by boiling concentrated hydrochloric and sulphuric acids, but is attacked by a hot mixture of fuming nitric acid and bromine. The aqueous solution gives a yellow coloration with ferric chloride solution. On exposure to air, the white solid assumes a yellowish-brown colour.

The filtrate from the preparation of sodium sulphoxylate, which still possessed a strong unpleasant odour, was found to contain salts of trithionic, sulphoxylic, and sulphuric acids, and also small quantities of penta- and possibly tetra-thionic acids. The product of the reaction between sulphur sesquioxide and sodium ethoxide has a strongly alkaline reaction and under these conditions it would be expected that any tetra- and penta-thionates formed would decompose with the formation of sulphites and thiosulphates, but the absence of the latter clearly proved that very little, if any, of these substances had been produced in the initial reaction.

The reactions which take place may be represented as follows :

(1) $S_2O_3 = SO + SO_2$.
(2) $SO + NaOEt = NaEtSO_2$.
(3) $NaEtSO_2 + NaOH = Na_2SO_2 + EtOH$.

Some of the sulphur monoxide or sesquioxide may react thus :

(4) $SO + 2SO_2 + NaOEt = NaEtS_3O_6$ or
(4a) $S_2O_3 + SO_2 + NaOEt = NaEtS_3O_6$.
(5) $NaEtS_3O_6 + NaOH = Na_2S_5O_6 + EtOH$.

The very small quantity of pentathionate present may be formed by the polymerisation of the sulphur monoxide :

(6) $5SO + NaOEt = NaEtS_5O_6$.
(7) $NaEtS_5O_6 + NaOH = Na_2S_5O_6 + EtOH$

or more probably by the decomposition of the trithionate :

(6a) $5Na_2S_3O_6 = Na_2S_5O_6 + Na_2S_4O_6 + 3Na_2SO_4 + 3SO_2$

(compare Debus, *loc. cit.*). The unpleasant odour of the solution may be due to the sodium ethyl salts present.

Attempt to isolate Sulphur Monoxide, SO.—Divers and Shimosé (*Ber.*, 1883, **16**, 1009) showed that the analogous tellurium compound, tellurium sulphoxide, $STeO_3$, decomposes when gradually heated in a vacuum to 235° with the production of tellurium monoxide; $STeO_3 = TeO + SO_2$, as confirmed by J. J. Doolan and one of us (J., 1924, **125**, 1403). It was possible that a similar reaction might take place with sulphur sesquioxide, although it was expected that the resulting sulphur monoxide would, if formed, be very much less stable. Sulphur sesquioxide was placed in a small Jena flask, and the latter exhausted to a pressure below 1 mm. of mercury. The flask was then gradually heated in a metal bath. As the temperature rose, the bluish-green solid slowly changed colour and signs of appreciable decomposition were apparent at about 70° : decomposition was complete at 95°. On further heating, the residue melted to an amber-coloured liquid which exhibited all the properties of sulphur.

It is possible that by employing a slower rate of heating in a very high vacuum from which all traces of moisture and oxygen have been excluded, sulphur monoxide might be isolated.

The "Colloidal Solution" Theory.—Although in the light of the experiments described in this paper there is little doubt that the bluish-green solid obtained by the interaction of sulphur and liquid sulphur trioxide is a definite chemical compound and not a "colloidal solution," it was considered advisable to obtain further evidence

against the latter view. Stress must be laid on the fact that pure sulphur is *insoluble* in pure sulphuric anhydride, although combination occurs with the formation of sulphur sesquioxide, which is also practically insoluble. It is only in the presence of small quantities of water that the substance dissolves to a blue solution.

Liquid sulphuric anhydride was added to sulphur contained in a glass tube, no precautions being taken to exclude moisture. After the violent reaction was over, the blue solution was poured off. An intense beam of light from a lantern was passed through the solution, but no Tyndall cone was visible.

If concentrated sulphuric acid be added gradually to the blue solution, and the latter examined after each addition for a Tyndall cone, it will be found that at a certain point corresponding to the green and brown solutions a marked Tyndall cone is visible, indicating that a substance (sulphur) of ultramicroscopic dimensions has separated. Further addition of sulphuric acid results in the separation of sulphur in a form visible to the naked eye.

Some of the blue liquid was carefully poured into water, and the resultant solution filtered from the precipitated sulphur. The filtrate contained trithionic acid (the main constituent), penta- and possibly tetra-thionic acids, sulphurous, sulphoxylic and sulphuric acids. If the deep blue solution be poured into a concentrated solution of potassium acetate, large quantities of potassium trithionate and little, if any, potassium tetra- and penta-thionates are present in the solution. It appears, therefore, that the tetra- and penta-thionates are produced from trithionates and nascent sulphur. Similar results are obtained with the green and brown solutions. One can accordingly conclude that the blue liquid is a *molecular* solution of sulphur sesquioxide in oleum, whilst the other coloured liquids produced by the dissolution of sulphur in fuming sulphuric acid of certain strengths are mixtures of colloidal solutions of sulphur and molecular solutions of sulphur sesquioxide.

In conclusion, the authors express their indebtedness to the Chemical Society for a grant which has partly defrayed the expenses incurred in the research.

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University of London. [*Received, May 26th*, 1925.]

CCIII.—*The Parachor and Chemical Constitution. Part I. Polar and Non-polar Valencies in Unsaturated Compounds.*

By SAMUEL SUGDEN, JOHN BRENT REED, and HENRY WILKINS.

(1) *Double Bonds and the Parachor.*

A NEW method of comparing molecular volumes by the use of a constant termed the "parachor" has been suggested by one of us (Sugden, J., 1924, **125**, 1177), who showed that this quantity is an additive function of certain atomic and structural constants by means of which the experimental values for a large number of organic compounds can be predicted with considerable accuracy.

Amongst the structural constants there evaluated is the effect of a double bond, which was found to add 23·2 units to the molecular parachor. Some of the data for this type of linking are given in Table I. The values of $[P]$ obs. given in the fourth column are calculated from observations by the investigators indicated by initials in the third column; full references are tabulated on p. 1535. The fifth column, headed $\Sigma[P]$, gives the sum of the atomic constants, and by subtracting this from the observed parachor the constant for the double bond in the last column is obtained.

TABLE I.

Parachor of non-polar double bonds.

Substance.	Formula.	Observer.	$[P]$ obs.	$\Sigma[P]$.	Double bond.
Ethylene	C_2H_4	M. & W.	99·5	78·0	21·5
Propylene	C_3H_6	,,	139·9	117·0	22·9
Amylene	C_5H_{10}	Sch.	218·2	195·0	23·2
Diallyl	C_6H_{10}	,,	248·2	199·8	$2 \times 24·2$
Acetone	C_3H_6O	M. & O.	160·9	137·0	23·9
Methyl ethyl ketone	C_4H_8O	,,	198·2	176·0	22·2
Diethyl ketone	$C_5H_{10}O$	,,	236·2	215·0	21·2
Methyl propyl ketone	,,	M. & S.	238·0	,,	23·0
Dipropyl ketone	$C_7H_{14}O$	M. & K.	314·1	293·0	21·1
Methyl hexyl ketone	$C_8H_{16}O$	M. & O.	355·7	332·0	23·7

This type of double linking has been found in a large number of organic compounds and gives an average increase of 23·2 units in the molecular parachor. The same value is found for double bonds between carbon and carbon, carbon and oxygen, carbon and sulphur, and nitrogen and oxygen atoms.

We have recently investigated a number of compounds of nitrogen, phosphorus, and sulphur, and have found several anomalous cases in which the presence of a double bond appears to have little or no effect on the parachor. The nitrogen compounds will be discussed

later; data for nine compounds of phosphorus and sulphur which show this anomaly are collected in Table II.

The atomic parachors for phosphorus and sulphur used in this table are $P = 37{\cdot}7$, and $S = 48{\cdot}2$; data on which they are based are presented on p. 1533. These values are consistent with those found for neighbouring elements in the periodic table

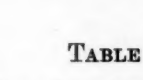
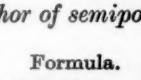
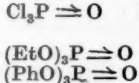
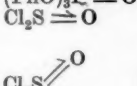
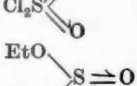
C.	N.	O.	F.	Si.	P.	S.	Cl.
4·8	12·5	20·0	25·7	12·0	37·7	48·2	54·3

and indicate a periodic variation of atomic parachors with increasing atomic number similar to the well-known property of atomic volume.*

The data presented in Tables I and II provide definite experimental evidence of the existence of two kinds of double bond, one, common in carbon compounds, but found also in compounds of other elements, which causes an increase in the parachor of 23·2 units, and another, present in derivatives of the oxyacids of sulphur and phosphorus, which lowers the molecular parachor by 1·6 units.

TABLE II.

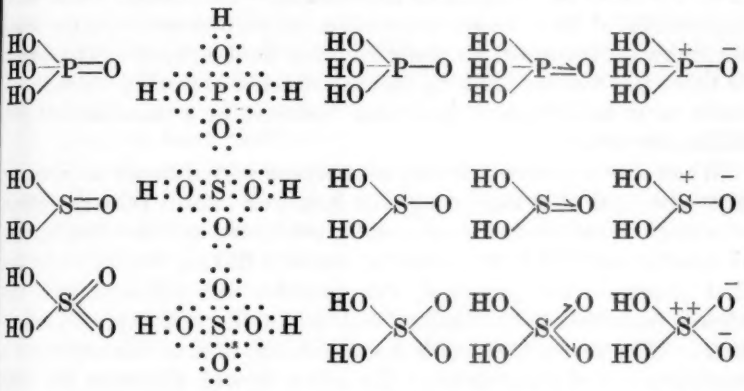
Parachor of semipolar double bonds.

Substance.	Formula.	Observer.	[P] obs.	Σ[P].	Double bond.
Phosphorus oxychloride	$Cl_3P \rightleftharpoons O$	S. R. & W.	217·6	220·6	− 3·0
		R. & S.	217·6	,,	− 3·0
Triethyl phosphate	$(EtO)_3P \rightleftharpoons O$	S. R. & W.	399·1	403·0	− 3·9
Triphenyl phosphate ...	$(PhO)_3P \rightleftharpoons O$	,,	686·5	687·7	− 1·2
Thionyl chloride	$Cl_2S \rightleftharpoons O$	,,	174·5	176·8	− 2·3
		R. & S.	(172·5)	,,	(− 4·3)
Sulphuryl chloride		S. R. & W.	193·3	196·8	− 1·65×2
		R. & S.	(187·0)	,,	(4·9×2)
Diethyl sulphite		W. & S.	299·7	298·4	+ 1·3
Ethyl ethanesulphonate		,,	295·8	,,	− 1·3×2
Dimethyl sulphate		S. R. & W.	238·9	240·4	− 0·75×2
Diethyl sulphate		,,	313·8	318·4	− 2·3×2
				Mean	− 1·6

* The variation of the parachor with atomic number will be discussed more fully in a subsequent paper.

(2) *Electron Valency Theories.*

The compounds discussed in Table II belong without exception to the class in which the octet valency theories of Lewis (*J. Amer. Chem. Soc.*, 1916, **38**, 762) and Langmuir (*ibid.*, 1919, **41**, 868, 1543; 1920, **42**, 274) lead to a modification of the usual structural formulæ. The electronic formulæ for phosphoric, sulphurous, and sulphuric acids are indicated in formulæ II; if a valency bond is written for each pair of shared electrons, then formulæ III are obtained which



(I.) (II.) (III.) (IV.) (V.)

do not exhibit the double bonds found in the usual formulæ I. It has been pointed out by Lowry (*Trans. Faraday Soc.*, 1923, **18**, 285) that in formulæ II the oxygen atom sharing two valency electrons and holding six others will be negatively charged and that, therefore, a double bond is present but consists of one covalency and one electrovalency. Lowry suggests two methods (IV and V) of formulating this type of linking; we have in most cases used the first of these methods in which a barb on the valency bond indicates the direction in which an electron has been transferred. This choice was largely determined by the consideration that formulæ of type V are apt to be confused with other formulæ in current use in which + and − signs are attached to atoms without removing a valency bond and so do not indicate an electrovalency.

Lowry has proposed the terms "mixed" or "ionised" double bonds for the linking present in formulæ IV and V. The second of these has been criticised by Porter, and by Rankine (*Trans. Faraday Soc.*, 1923, **18**, 296) on the grounds that no free ions are present, and the term "mixed" is somewhat indefinite. The nomenclature of Lewis (*loc. cit.*) for the two kinds of single bond, namely, polar valencies and covalencies, is now in common use, and in conformity with this we propose to term the double bond

consisting of one covalency and one electrovalency a semipolar double bond. The linking commonly found in carbon compounds which consists of two covalencies will be termed a non-polar double bond.

That two kinds of double bond do exist is shown clearly by the experimental evidence summarised in Tables I and II. Further, from the fact that all the substances in Table II must, on the octet theory, contain semipolar double bonds it is evident that a parachor of — 1·6 must be assigned to this linking. The double bond with a parachor of 23·2 which is common in carbon compounds must therefore be identified as the non-polar double bond. The effect of these two types of linking on the parachor is readily understood when it is remembered that this constant is a measure of the molecular volume.

When any additive relation is analysed and reduced to a series of atomic and structural constants it is well known that the effect of a single bond cannot be separately evaluated and the assumption is usually made that the constant for this linking is zero. In the first paper on the parachor, this practice was followed and the atomic parachors there obtained include the effect, if any, of a single bond. The semipolar double bond consists of a covalency with a superimposed electrovalency; its effect should therefore be that of a single bond, which is taken as zero, plus the effect of the electrostatic attraction between the two charged atoms, which should cause a contraction in volume. This contraction would not be large, since it appears improbable that considerable distortion of the outer shells of electrons could occur. It is significant that with one exception all the substances in Table II give a negative value for the parachor of a semipolar double bond. The mean value, — 1·6, is of the same order of magnitude as the deviations of individual values from this mean, but the balance of evidence seems to be in favour of a real but small negative value for the contribution of this linking to the parachor.

For the non-polar double bond there is the large expansion in volume of 23·2 units. The original cubical atom of Lewis (*loc. cit.*) would give a smaller volume for two cubes placed face to face than for two cubes edge to edge. The statical theory of atomic structure is, however, quite incapable of accounting for all the modern work on spectra and atomic structure and in particular the successful application of relativity considerations to the explanation of the fine structure of spectral lines seems to provide conclusive evidence in favour of the dynamical theory. On this view, the large expansion in volume caused by a non-polar double bond indicates that when four shared electrons move in orbits around or between the

two atoms which share them the mutual interactions of the electrons thus crowded together lead to a looser structure of the molecule as a whole.

It should be emphasised here that, with this exception, none of the results of the Lewis-Langmuir theory discussed in the present paper is concerned with the assumption of a cubical atom or of a statical theory of atomic structure. All the deductions with regard to valency follow from two postulates: (*a*) that a covalency consists of two shared electrons, and (*b*) that the maximum number of electrons in the outer shell of any atom is eight. The latter assumption is limited to the first two periods of the periodic table by Langmuir, who, for elements of higher atomic number, postulates the existence of a greater number of electrons in the outer shell. This view has been modified by Bury (*J. Amer. Chem. Soc.*, 1921, 43, 1602), who retains the outer shell of eight for all the inert gases, whilst Bohr's theory of atomic structure ("The Theory of Spectra and Atomic Structure," Cambridge University Press, 1922) retains eight electrons of greatest total quantum number, which may be regarded as valency electrons.

In this connexion the recent measurements of von Wartenberg (*Annalen*, 1924, **440**, 97) of the surface tension and density of osmium tetroxide are of considerable interest, as they provide an experimental test of the truth of the octet theory for an element of high atomic number. From these data, the parachor for osmium tetroxide is 154·0. On the assumption that the oxygens are held by four semipolar double bonds giving an outer shell of eight electrons, the parachor for osmium is 80·4; if the osmium atom in this compound has an outer shell of sixteen electrons, and four non-polar double bonds are present, then the parachor for osmium becomes − 18·8. Although there are no further data on osmium compounds available from which an independent value of the parachor can be obtained, it will be seen from the rough values for neighbouring elements given below that the value $Os = 80$ falls into place in the series which exhibits a minimum at gold. Hence it appears probable that osmium tetroxide has the structure $Os(\rightleftharpoons O)_4$ and that the octet rule may hold for elements of high atomic number as well as for the first two periods of the table.

Element	Os	Ir	Pt	Au	Hg	Tl	Pb	Bi
Atomic number	76	77	78	79	80	81	82	83
Parachor	80	—	68	54	70	—	90	92
Observer	—	—	Q.	Hey.	H.	—	H.	H.

In most of his formulæ Langmuir assumes wherever possible the formation of complete octets; in later theories (Latimer and Rodebush, *J. Amer. Chem. Soc.*, 1920, **42**, 1419), the existence of

sextets is postulated in certain cases. In particular, Lowry (J., 1923, **123**, 822) has suggested that most double bonds are semi-polar and states that " a double bond in organic chemistry usually reacts as if it contained one covalency and one electrovalency." This view has been criticised on stereochemical grounds (Sugden, *ibid.*, p. 1861; Farmer, *ibid.*, p. 2531) and, so far as the normal state of the molecule is concerned, it seems necessary to retain the conception of the non-polar double bond to account for the existence of geometrical isomerides. We have now, in the parachor, a method of determining experimentally what type of linking is present in a particular molecule, and the remainder of the present paper will be devoted to the discussion of the constitution of a number of unsaturated compounds of carbon, nitrogen, phosphorus, and sulphur for which experimental values of this constant are available.

(3) *Carbon Compounds.*

The non-polar double bond contributing 23·2 units to the molecular parachor appears, so far, to be the only type of double linking in which the carbon atom takes part. It has been found in more than one hundred carbon compounds including hydrocarbons, aldehydes, ketones, and esters. In particular, it may be mentioned that five pairs of geometrical isomerides recently examined in this laboratory have all been found to possess this type of linking.*

The case of the carbonates is of special interest. Langmuir gives the usual formula $(RO)_2C{=}O$ and points out that carbonates are not isomorphous with sulphites, which, on Lowry's method of formulation, have the structure $(RO)_2S{\rightleftharpoons}O$. On the other hand, Lowry suggests that the stability of oxyacids depends upon the presence of a positively charged nuclear atom and writes the carbonate ion $\ddot{O}{-}\overset{+}{C}\begin{matrix}\diagup\ddot{O}\\ \\ \diagdown\ddot{O}\end{matrix}$. We have therefore measured the surface tension and density of two esters of carbonic acid with the following results :

	[*P*] obs.	[*P*] calc. Non-polar.	[*P*] calc. Semipolar.
Diethyl carbonate	277·4	278·2	253·4
Diphenyl carbonate	467·4	468·0	443·2

It is evident that these compounds contain a non-polar double bond.

(4) *Nitrogen Compounds.*

The structure of nitrous acid presents the same ambiguity as that of carbonic acid. Langmuir gives the formula $RON{=}O$, whilst

* The data for these substances will be presented in a later paper.

Lowry assumes that a semipolar double bond is present and writes the nitrite ion $\bar{O}—\overset{+}{N}—\bar{O}$. We have therefore examined two esters of nitrous acid; it will be seen from the values found for the parachor that Langmuir's formula is correct and that the esters of nitrous acid, like those of carbonic acid, do not contain a positively charged nuclear atom.

	[P] obs.	[P] calc. Non-polar.	[P] calc. Semipolar.
n-Butyl nitrite	251·8	248·8	224·0
*iso*Amyl nitrite	287·4	287·8	263·0

The existence of two types of double bond gives no fewer than four possible formulæ for the nitro-group. These formulæ together with the corresponding values of the parachor for the group NO_2 are given below. Formula (VI) is of course excluded by the c tet

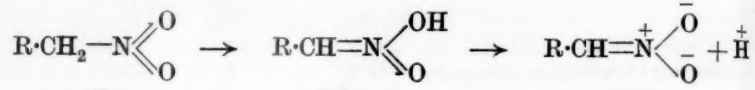
98·9 (VI.) 74·1 (VII.) 49·3 (VIII.) 69·5 (IX.)

theory, and Langmuir adopted (VII) for this group, whilst Latimer and Rodebush and Lowry give the symmetrical formula (VIII). In the first paper on the parachor, it was pointed out that the experimental figures for this group were much smaller than would be expected for (VI) and it was assumed that the nitro-group possessed the alternative cyclic structure (IX). If this view is accepted, then from the experimental figures for nitro-compounds the constant for a three-membered ring is 21·5. An investigation of derivatives of *cyclo*propane and of ethylene oxide is now in progress, and the results so far obtained indicate that this value is too high and that the constant for a three-membered ring is approximately 17 units; this figure has been used in calculating the parachor given under (IX). The experimental data for nitro-compounds are tabulated below; the mean value of 74·2 is very close to the figure calculated for (VII), and (VI) and (VIII) are certainly excluded. The difference between (VII) and (IX) is not very large; the balance of evidence

Substance.	Formula.	Observer.	[P] obs.	Σ[P].	NO_2
Nitrogen peroxide	$NO_2{\cdot}NO_2$	R. & S.	144·4	0	72·2
Nitromethane	$CH_3{\cdot}NO_2$	M. & S.	132·0	56·1	75·9
		H. C. & R.	132·1	,,	76·0
Ethyl nitrate	$C_2H_5{\cdot}O{\cdot}NO_2$	M. & S.	189·6	115·1	74·5
Nitrobenzene	$C_6H_5{\cdot}NO_2$	S.	264·5	190·0	74·5
p-Nitrotoluene	$C_7H_7{\cdot}NO_2$	,,	302·8	229·0	73·8
p-Nitrochlorobenzene ...	$C_6H_4Cl{\cdot}NO_2$	,,	300·0	227·2	72·8
				Mean	74·2

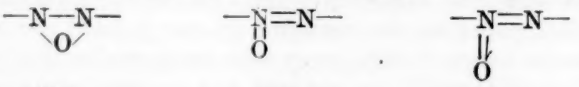
is in favour of (VII), although (IX) cannot be entirely excluded until the constant for a three-membered ring has been investigated more

fully. On chemical grounds, the Langmuir formula (VII) is to be preferred to the cyclic formula, as it suggests an explanation of the production of an *aci*-form from primary and secondary nitro-paraffins as indicated in formulæ (X), (XI), and (XII). On this view the ion of the ψ-acid has the symmetrical formula (XII) suggested by Lowry, whilst the original nitro-compound contains only one semipolar double bond.



(X.) (XI.) (XII.)

Azoxy-compounds were at one time supposed to have the structure shown in (XIII). The existence of pairs of isomerides of a number of unsymmetrical azoxy-compounds (Angeli, *Ahrens Vort.*, 1913, **19**, 447) has led to the adoption of formula (XIV), which is, however, impossible on the octet theory, since the nitrogen atom is quinque-covalent. One of the double bonds must be semipolar and from electrochemical considerations and from the fact that azoxy-compounds are readily formed by the oxidation of azo-compounds it appears probable that this is the linking between nitrogen and



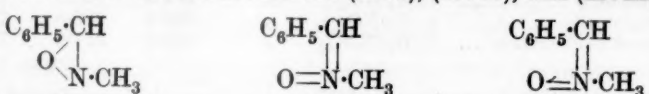
62·0 91·2 66·7
(XIII.) (XIV.) (XV.)

oxygen as shown in (XV). We have examined azoxybenzene and *o*-azoxytoluene with the following results :

	[*P*] obs.	Σ[*P*].	N_2O.
Azoxybenzene	444·7	380·0	64·7
o-Azoxytoluene	528·6	458·0	70·6

If Angeli's evidence for excluding formula (XIII) is accepted, these results give a satisfactory confirmation of (XV).

We are indebted to Dr. O. L. Brady for the loan of specimens of the *N*- and *O*-methyl ethers of benz*anti*aldoxime, the measurement of which has given the following results : *O*-Methyl ether, [*P*] obs. = 324·2; *N*-methyl ether, [*P*] obs. = 325·9. The *O*-ether must have the structure $C_6H_5{\cdot}CH{:}N{\cdot}O{\cdot}CH_3$, for which [*P*] calc. = 323·7, in good agreement with the observed value. For the *N*-ether the structures indicated in formulæ (XVI), (XVII), and (XVIII) are



317·5 346·9 321·2
(XVI.) (XVII.) (XVIII.)

possible. Here, again, the parachor confirms the octet theory in excluding formulæ such as (XVII) in which nitrogen is quinquecovalent. The observed figure, whilst rather high, is in favour of the modified nitrone structure (XVIII) with a semipolar double bond between nitrogen and oxygen.

The investigation of other types of quinquevalent nitrogen compounds will obviously be of considerable interest, and we hope to extend our work in this direction in the near future. For the three types so far examined, namely, nitro-compounds, azoxy-compounds, and *N*-oximino-ethers, the parachor confirms completely Langmuir's contention that the maximum covalency of nitrogen is four, the fifth valency, as pointed out by Lowry, being always an electrovalency.

(5) *Phosphorus Compounds.*

The following table contains the data from which the parachor for phosphorus has been deduced and does not call for further comment :

Substance.	Formula.	Observer.	[*P*] obs.	Σ[*P*].	Phosphorus
Phosphorus trichloride	PCl_3	M. & D.	199·0	162·9	36·1
		R. & S.	201·1	,,	38·2
Phosphorus tribromide...	PBr_3	S. R. & W.	242·9	204·0	38·9
Triphenylphosphine	$P(C_6H_5)_3$	W. & S.	607·7	570·0	37·7
					Mean 37·7

Data for phosphorus oxychloride and for two esters of phosphoric acid are contained in Table II. In accordance with the octet theory the double bond in these compounds is of the semipolar type.

(6) *Sulphur Compounds.*

The following table contains the data from which the parachor for sulphur has been calculated :

Substance.	Formula.	Observer.	[*P*] obs.	Σ[*P*].	Sulphur
Sulphur monochloride ...	S—Cl | S—Cl	R. & S.	205·1	108·6	48·2
Carbon disulphide	S=C=S	,,	144·7	51·2	46·8
		M. & T.	143·6	,,	46·2
		M. & D.			
		H. C. & R.	142·9	,,	45·9
Ethyl mercaptan	C_2H_5·SH	M. & C.	162·9	112·2	50·7
Phenyl mercaptan.....	C_6H_5·SH	W. & S.	257·5	207·1	50·4
		M. & C.	256·4	,,	49·3
					Mean 48·2

The data for the acid chlorides and esters of sulphurous and sulphuric acids are contained in Table II; in accordance with the requirements of the octet theory these compounds all contain semipolar double bonds.

Data for a few thiocyanates and thiocarbimides are available and

present some points of interest. The table below shows that the double and triple bonds in these compounds are all of the non-polar type, since the values of [*P*] calc. obtained on this assumption are in good agreement with the observed figures. The double bonds in carbon disulphide also are non-polar, hence the absence of such bonds in sulphites and sulphates cannot be ascribed to an intrinsic property of the sulphur atom which prevents the formation of normal linkings.

Substance.	Formula.	Observer.	[*P*] obs.	[*P*] calc.
Methyl thiocyanate	$CH_3{\cdot}S{\cdot}C{\vdots}N$	Sch.	168·6	168·2
Ethyl thiocyanate	$C_2H_5{\cdot}S{\cdot}C{\vdots}N$	R. & S.	210·7	207·2
		M. & C.	209·1	,,
Ethylthiocarbimide	$C_2H_5{\cdot}N{:}C{:}S$	,,	211·7	207·0
Allylthiocarbimide	$C_3H_5{\cdot}N{:}C{:}S$	,,	232·4	235·0
Phenylthiocarbimide	$C_6H_5{\cdot}N{:}C{:}S$	,,	304·1	301·9

Ethyl thiocyanate and ethylthiocarbimide have almost exactly the same parachor. This is further evidence for the value 46·6 for the triple bond (deduced from nitriles and acetylene derivatives), which is almost exactly twice the constant for a non-polar double bond (23·2). This suggests that each covalency in a multiple bond adds 23·2 units except the first one, which has no effect on the parachor.

In conclusion, it should be stated that in the present paper we are considering only the structure of the molecule in the " resting " state, whilst some of the formulæ discussed above (particularly those of Lowry) are intended to refer to the " reactive " condition. The arrangement of the atoms in the molecule in the " resting " state expressed in the structural formula is fundamental, not only for stereochemistry and for the discussion of physical properties, but as a basis for the consideration of the structure of the molecule in the " reactive " state. The structure of the activated molecule, if it differs perceptibly from that of the inactive molecule, must be simply related to it. We have shown in the present paper that whilst semipolar double bonds do occur in certain compounds they are not found in the non-activated molecules of carbon compounds generally. Lowry's hypothesis concerning carbon compounds may therefore be taken to mean that the activation of such compounds consists in the transference of an electron whereby a non-polar double bond is converted into one of the semipolar type. This view does give a simple connexion between the structures in the activated and non-activated states; it is beyond the scope of the present paper to discuss whether this hypothesis gives a satisfactory picture of the nature of the change involved in the process of activation. So far as the non-activated molecules are concerned, one general rule holds. Semipolar double bonds are only formed when each

atom except hydrogen has attained a complete octet and when the formation of a non-polar double bond would cause one or other of the atoms concerned to be associated with more than eight electrons, or, in other words, to have a covalency greater than four.

Summary.

(1) By means of the parachor the existence of two types of double bond has been demonstrated experimentally.

(2) These are identified as the non-polar and semipolar double bonds predicted by the octet theory as developed by Lewis, Langmuir, and Lowry.

(3) The nature of the double linking in a number of compounds of carbon, nitrogen, phosphorus, and sulphur has been investigated. In all the cases so far examined, semipolar double bonds are formed only when each atom, except hydrogen, has attained a complete octet. The octet is never exceeded and semipolar bonds are not found when their existence would necessitate the presence of a sextet around one or other of the atoms concerned. Sextets must be present in a few cases, as in the ion of triphenylmethyl chloride, but such structures are apparently rare.

(4) There is some evidence that the octet rule is not restricted to elements of the first two periods of the periodic table, but that it may hold for elements of higher atomic number.

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Experimental.

New measurements have been made of the surface tension and density of sixteen substances, the former by the method of maximum bubble pressure (Sugden, J., 1922, **121**, 858; 1924, **125**, 27) and densities by means of the U-shaped pyknometer described in

the second of these papers. Three bubblers were used, the constants for which are given below:

App.	8b.	8c.	4d.
r_2	0·206	0·206	0·139 cm.
A	0·003730	0·005622	0·007767

In the tables below, the first column gives the apparatus used and the second column the temperature. The thermometers used were compared with a reference standard calibrated at the National Physical Laboratory and the observations are corrected for exposed stem. The difference of the pressures (expressed in dynes/cm.^{2}) required to liberate bubbles from the two tubes of the bubbler is given under P, D is the density of the liquid in g./c.c., and ϕ a correction factor calculated by the formula $\phi = 1 + 0{\cdot}69r_2gD/P$, where r_2 is the radius of the wide tube in cm. and $g = 981$ cm./sec.^{2}. γ is the surface tension in dynes/cm. calculated by the equation $\gamma = AP\phi$, where A is the apparatus constant determined by experiments with benzene. The parachor in the last column is then obtained by the expression $[P] = \gamma^{1/4}M/(D - d)$, where M is the molecular weight and d the density of the vapour in g./c.c. In most cases d is very small compared with D and can be neglected except at temperatures approaching the boiling point. A method of calculating approximate values of the vapour density is given as an appendix to this paper, and has been used in those cases in which $D - d$ has been placed at the head of column 4 in the tables below.

Ethyl carbonate was twice fractionally distilled; the portion used boiled at 125·2—125·8° (corr.)/756 mm. Densities determined: $D_4^{13°}$ 0·974, $D_4^{26°}$ 0·959, $D_4^{42°}$ 0·941, $D_4^{56·5°}$ 0·925; whence $D_4^{t°} = 0{\cdot}988 - 0{\cdot}00113t$. Molecular weight 118·1.

App.	t.	P.	D.	ϕ.	γ.	Parachor.
4d	13°	3425	0·973	1·0268	27·30	277·5
,,	33	3112	0·951	1·0288	24·86	277·3
,,	43·5	2965	0·939	1·0298	23·71	277·5
,,	65·5	2640	0·914	1·0326	21·17	277·2
						Mean 277·4

Phenyl carbonate was recrystallised from absolute alcohol and melted sharply at 79·5° (corr.). Densities determined: $D_4^{87°}$ 1·1215, $D_4^{111°}$ 1·0997, $D_4^{145°}$ 1·0690; whence $D_4^{t°} = 1{\cdot}2002 - 0{\cdot}000905t$. Molecular weight 214·1.

App.	t.	P.	D.	ϕ.	γ.	Parachor.
4d	101°	4308	1·1089	1·0242	34·28	467·2
,,	120·5	4041	1·0912	1·0254	32·19	467·3
,,	139	3815	1·0744	1·0264	30·41	467·8
						Mean 467·4

n-*Butyl nitrite* was prepared from *n*-butyl alcohol and repeatedly fractionated. The specimen used boiled at 75—76° (corr.)/768 mm.

Densities determined : $D_4^{11°}$ 0·8928, $D_4^{26°}$ 0·8756, $D_4^{44·5°}$ 0·8534; whence $D_4^{t°} = 0·9059—0·001176t$. Molecular weight 103·1.

App.	t.	P.	$D - d$.	ϕ.	γ.	Parachor.
4d	13°	2781	0·8901	1·0301	22·25	251·5
,,	28·5	2555	0·8716	1·0321	20·48	251·6
,,	42·5	2380	0·8547	1·0338	19·12	252·1
,,	56·5	2184	0·8375	1·0361	17·58	252·0
					Mean	251·8

iso*Amyl nitrite* was prepared from Kahlbaum's *iso*amyl alcohol and was repeatedly fractionated. The specimen used boiled at 98·5—99·5° (corr.)/768 mm. Densities determined : $D_4^{13·5°}$ 0·885, $D_4^{44·5°}$ 0·864, $D_4^{74°}$ 0·820; whence $D_4^{t°} = 0·900—0·00108t$.

App.	t.	P.	$D - d$.	ϕ.	γ.	Parachor.
4d	14°	2821	0·885	1·0295	22·04	286·7
,,	35	2539	0·862	1·0320	20·35	288·5
,,	56	2247	0·839	1·0350	18·06	287·7
,,	73	2019	0·820	1·0380	16·28	286·8
					Mean	287·4

Azoxybenzene was recrystallised from ligroin and melted at 35·0—35·5° (corr.). Densities determined : $D_4^{44°}$ 1·150, $D_4^{36·5°}$ 1·132, $D_4^{78·5°}$ 1·122, $D_4^{91·5°}$ 1·109; whence $D_4^{t°} = 1·189—0·000864t$. Molecular weight 198·2.

App.	t.	P.	D.	ϕ.	γ.	Parachor.
8b	51°	11460	1·145	1·0140	43·34	444·0
,,	66·5	10945	1·132	1·0144	41·42	444·0
,,	77·5	10637	1·122	1·0147	40·26	444·8
,,	89	10356	1·112	1·0150	39·17	445·8
					Mean	444·7

o-*Azoxytoluene* was recrystallised from ligroin and melted at 58—59° (corr.). Densities determined : $D_4^{74°}$ 1·0768, $D_4^{83°}$ 1·0698, $D_4^{91°}$ 1·0637, $D_4^{125·5°}$ 1·0369, $D_4^{139°}$ 1·0248; whence $D_4^{t°} = 1·1353—0·000790t$. Molecular weight 226·2.

App.	t.	P.	D.	ϕ.	γ.	Parachor.
8b	69·5°	10686	1·0804	1·0141	40·41	527·9
,,	78·5	10412	1·0733	1·0144	39·39	528·0
,,	90·5	10130	1·0638	1·0146	38·33	529·0
,,	101	9839	1·0555	1·0150	37·25	529·4
					Mean	528·6

O-*Methyl ether* of benz*anti*aldoxime. The specimen supplied by Dr. O. L. Brady was distilled immediately before measurement and boiled at 197—199° (corr.)/762 mm. Densities determined : $D_4^{14·5°}$ 1·0325, $D_4^{39·5°}$ 1·0165, $D_4^{51·5°}$ 0·9967, $D_4^{72°}$ 0·9757; whence $D_4^{t°} = 1·0465—0·000976t$. Molecular weight 135·1.

App.	t.	P.	D.	ϕ.	γ.	Parachor.
4d	16·5°	4670	1·0304	1·0208	37·03	323·4
,,	33·5	4399	1·0138	1·0217	34·92	324·3
,,	55·5	4052	0·9923	1·0230	32·20	324·4
,,	73	3788	0·9753	1·0242	30·13	324·6
					Mean	324·2

N-*Methyl ether* of benz*anti*aldoxime. The specimen supplied by Dr. O. L. Brady melted sharply at 84° (corr.). Densities determined : $D_{4^\circ}^{103^\circ}$ 1·0505, $D_{4^\circ}^{120^\circ}$ 1·0357, $D_{4^\circ}^{135\cdot5^\circ}$ 1·0236, $D_{4^\circ}^{151^\circ}$ 1·0117; whence $D_{4^\circ}^{t^\circ} = 1\cdot1333—0\cdot000808t$. Molecular weight 135·1.

App.	*t*.	*P*.	*D*.	ϕ.	γ.	Parachor.
4d	100°	5171	1·0525	1·0192	40·93	324·7
,,	122	4875	1·0347	1·0200	38·62	325·4
,,	141	4641	1·0194	1·0207	36·80	326·4
,,	163	4352	1·0016	1·0216	34·53	327·0
					Mean	325·9

Phosphorus tribromide was repeatedly fractionated first at ordinary pressure and finally under reduced pressure. The specimen used boiled at 66·5° (corr.)/20 mm. and at 176—177° (corr.)/772 mm. Some difficulty was experienced in measuring the surface tension of this substance owing to the presence of an orange-coloured impurity which separated slowly and blocked the capillary. This was not removed by repeated distillations at atmospheric pressure, but was left behind when the substance was distilled at 20 mm. A drying tube, 60 cm. long, filled with phosphorus pentoxide, was fitted above the bubbler to dry the incoming air. Densities determined : $D_{4^\circ}^{15^\circ}$ 2·904, $D_{4^\circ}^{33\cdot5^\circ}$ 2·860, $D_{4^\circ}^{52^\circ}$ 2·813, $D_{4^\circ}^{70\cdot5^\circ}$ 2·768; whence $D_{4^\circ}^{t^\circ} = 2\cdot942—0\cdot00247t$. Molecular weight 270·8.

App.	*t*.	*P*.	*D*.	ϕ.	γ.	Parachor.
4d	24°	5630	2·883	1·048	45·8	244·4
,,	33	5410	2·861	1·050	44·1	244·0
,,	59·5	4680	2·795	1·056	38·4	241·2
,,	72	4520	2·764	1·058	37·1	242·0
					Mean	242·9

Phosphorus oxychloride was twice distilled; the fraction used boiled at 108·6—108·8° (corr.)/769 mm. Densities determined : $D_{4^\circ}^{14\cdot5^\circ}$ 1·691, $D_{4^\circ}^{31\cdot5^\circ}$ 1·659, $D_{4^\circ}^{49\cdot5^\circ}$ 1·625; whence $D_{4^\circ}^{t^\circ} = 1\cdot718—0\cdot00188t$. Molecular weight 153·4.

App.	*t*.	*P*.	*D*.	ϕ.	γ.	Parachor.
8c	15°	5595	1·690	1·0421	32·77	217·1
,,	49	4819	1·626	1·0471	28·36	217·7
,,	65	4504	1·596	1·0494	26·57	218·1
					Mean	217·6

Triethyl phosphate was prepared by the method of Limpricht (*Annalen*, 1865, **134**, 347) and was fractionated twice under diminished pressure. The specimen used boiled at 108° (corr.)/25 mm. and, with slight decomposition, at 216° (corr.)/770 mm. Densities determined : $D_{4^\circ}^{15^\circ}$ 1·0794, $D_{4^\circ}^{38^\circ}$ 1·0551, $D_{4^\circ}^{92\cdot5^\circ}$ 1·0395, $D_{4^\circ}^{67^\circ}$ 1·0257, $D_{4^\circ}^{83^\circ}$ 1·0093; whence $D_{4^\circ}^{t^\circ} = 1\cdot0943—0\cdot001028t$. Molecular weight 182·2.

App.	t.	P.	D.	ϕ.	γ.	Parachor.
8c	15·5°	5294	1·0784	1·0284	30·61	397·7
,,	38·5	4887	1·0547	1·0301	28·30	398·4
,,	69·5	4383	1·0229	1·0325	25·44	400·1
,,	87·5	4067	1·0044	1·0344	23·65	400·1
					Mean	399·1

Triphenyl phosphate was recrystallised from a mixture of absolute alcohol and ligroin and melted sharply at 50° (corr.). Densities determined: $D_{4^\circ}^{58^\circ}$ 1·2055, $D_{4^\circ}^{68\cdot5^\circ}$ 1·1970, $D_{4^\circ}^{79\cdot5^\circ}$ 1·1883, $D_{4^\circ}^{99^\circ}$ 1·1803; whence $D_{4^\circ}^{t^\circ} = 1\cdot2523 - 0\cdot000807t$. Molecular weight 326·2.

App.	t.	P.	D.	ϕ.	γ.	Parachor.
4d	65·5°	5118	1·1994	1·0221	40·63	686·5
,,	74	4991	1·1926	1·0225	39·64	686·3
,,	84	4872	1·1845	1·0229	38·71	686·8
					Mean	686·5

Thionyl chloride was repeatedly fractionated; the specimen used boiled at 76·9—77·1° (corr.)/772 mm. Densities determined: $D_{4^\circ}^{14\cdot5^\circ}$ 1·656, $D_{4^\circ}^{32^\circ}$ 1·622, $D_{4^\circ}^{48^\circ}$ 1·593; whence $D_{4^\circ}^{t^\circ} = 1\cdot683 - 0\cdot00188t$. Molecular weight 119·0.

App.	t.	P.	$D - d$.	ϕ.	γ.	Parachor.
8c	18	5820	1·649	1·0395	34·01	174·3
,,	37	5375	1·613	1·0418	31·48	174·8
,,	51	4992	1·587	1·0443	29·31	174·4
					Mean	174·5

Sulphuryl chloride was prepared by boiling chlorosulphonic acid with a little mercuric sulphate and was repeatedly fractionated. The specimen used boiled at 70·0—70·2° (corr.)/772 mm. For the surface tension measurements the incoming air was dried over phosphorus pentoxide. Densities determined: $D_{4^\circ}^{12^\circ}$ 1·700, $D_{4^\circ}^{25^\circ}$ 1·671, $D_{4^\circ}^{38\cdot5^\circ}$ 1·640; whence $D_{t^\circ}^{t^\circ} = 1\cdot727 - 0\cdot00227t$. Molecular weight = 135·0.

App.	t.	P.	$D - d$.	ϕ.	γ.	Parachor.
4d	13°	4380	1·696	1·0364	35·26	193·9
,,	23·5	4081	1·673	1·0386	32·92	193·3
,,	47·5	3504	1·617	1·0434	28·40	192·8
					Mean	193·3

Dimethyl sulphate. The commercial product was distilled once under reduced pressure and fractionated at atmospheric pressure. The specimen used boiled at 187·5° (corr.)/769 mm. Densities determined: $D_{4^\circ}^{16\cdot5^\circ}$ 1·3367, $D_{4^\circ}^{38^\circ}$ 1·3093, $D_{4^\circ}^{59\cdot5^\circ}$ 1·2820, $D_{4^\circ}^{92\cdot5^\circ}$ 1·2533; whence $D_{4^\circ}^{t^\circ} = 1\cdot3575 - 0\cdot001265t$. Molecular weight 126·1.

App.	t.	P.	D.	ϕ.	γ.	Parachor.
4d	18°	5038	1·3347	1·0249	40·12	237·7
,,	36·5	4738	1·3113	1·0260	37·76	238·3
,,	55	4444	1·2879	1·0273	35·46	238·8
,,	74·5	4163	1·2632	1·0285	33·25	239·6
,,	93	3879	1·2399	1·0301	31·03	240·0
					Mean	238·9

Diethyl sulphate. The commercial product was twice distilled under diminished pressure; the specimen used boiled at 110°

(corr.)/30 mm. Densities determined: $D_4^{12°}$ 1·197, $D_4^{30·5°}$ 1·175, $D_4^{50·5°}$ 1·153, $D_4^{67°}$ 1·135; whence $D_4^{t°} = 1·210—0·00112t$. Molecular weight 154·1.

App.	t.	P.	D.	ϕ.	γ.	Parachor.
4d	13°	4344	1·195	1·0259	34·61	312·7
,,	32·5	4080	1·174	1·0271	32·54	313·5
,,	48	3866	1·156	1·0281	30·86	314·2
,,	70	3576	1·132	1·0298	28·60	314·8
					Mean	313·8

APPENDIX.

Calculation of Vapour Density in the Neighbourhood of the Boiling Point.—The expression for the parachor involves the quantity $D - d$ and whilst the vapour density, d, is small compared with D in most cases, it becomes sufficiently large to affect the value of the parachor at temperatures approaching the boiling point. The value of d can, however, be calculated in the following manner with sufficient accuracy, since it only enters into the expression for the parachor as a small correction term.

If it is assumed that the gas laws hold for the vapour at the boiling point, then $d_b = 0·0122M/T_b$, where d_b is the vapour density at the boiling point T_b on the absolute scale at 760 mm., whilst M is the molecular weight. For lower temperatures, the variation of the vapour density is expressed with sufficient accuracy by the expression $\log_{10} d/d_b = 5(T/T_b - 1)$, where d is the vapour density at an absolute temperature, T. The accuracy with which this empirical expression can be used to calculate the vapour density is shown by the examples below. The values of d obs. are those given by Young (*Proc. Roy. Soc. Dublin*, 1910, **12**, 374).

Benzene: $T_b = 353$, $d_b = 0·0027$.

t.	d calc.	d obs.	Diff.
80°	0·0027	0·0027	±0·0000
60	0·0014	0·0015	−0·0001
40	0·0007	0·0008	−0·0001
20	0·0004	0·0004	±0·0000

Chlorobenzene: $T_b = 405$, $d_b = 0·0034$.

t.	d calc.	d obs.	Diff.
120°	0·0024	0·0026	−0·0002
100	0·0014	0·0014	±0·0000
80	0·0008	0·0008	±0·0000
60	0·0004	0·0002	+0·0002

Diethyl ether: $T_b = 308$, $d_b = 0·0029$.

t.	d calc.	d obs.	Diff.
30°	0·0024	0·0027	−0·0003
20	0·0016	0·0019	−0·0003
10	0·0012	0·0013	−0·0001
0	0·0008	0·0008	±0·0000

Ethyl acetate: $T_b = 350$, $d_b = 0·0031$.

t.	d calc.	d obs.	Diff.
60°	0·0016	0·0018	−0·0002
40	0·0009	0·0008	+0·0001
20	0·0003	0·0003	±0·0000

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FETTER LANE, E.C. 4. [*Received, April 17th*, 1925.]

CCIV.—*The System Chromium Trioxide–Boric Acid–Water.*

By Lionel Felix Gilbert.

This investigation was undertaken in continuation of previous work on the interaction of chromic acid with other acids (Gilbert, Buckley, and Masson, J., 1922, **121**, 1935; Mumford and Gilbert, J., 1923, **123**, 471).

The general experimental method was similar to that previously described (*loc. cit.*). The reaction tubes were partly filled with chromic acid solutions of different concentrations and with approximately known amounts of (ortho-) boric acid. The temperatures were again 25° and 45°.

Chromic acid was estimated iodometrically; total acidity was determined by titration of another sample with barium hydroxide, mannitol being added when the end-point, indicated by phenolphthalein, was near. As the commercial mannitol used had a slightly acid reaction, it was found convenient to make up a saturated stock solution in water and to neutralise from time to time with barium hydroxide. A few c.c. of the saturated solution were sufficient for each titration. Baryta was run into each suitably diluted mixture till a definite pink colour persisted for 3 minutes (compare Kolthoff, *Chem. Weekblad*, 1922, **19**, 449). This end-point is, however, sometimes difficult to determine accurately.

The results obtained are shown in Tables I and II, boric acid

Table I.

Compositions (g. per 100 g.) and densities at 25°.

Liquid phase.			Wet solid.	
$d_4^{25°}$.	CrO_3.	B_2O_3.	CrO_3.	B_2O_3.
1·699	62·40	0·10	32·38	26·09
1·657	59·90	0·16	35·82	22·36
	53·72	0·28		
	49·75	0·42	45·39	5·28
1·420	43·80	0·65	24·42	24·89
	37·89	0·92	21·12	25·11
1·296	33·05	1·02	17·94	26·07
1·212	24·31	1·35	9·02	35·72
1·156	18·07	1·58	9·30	28·52
1·086	9·42	2·28	5·19	27·07
1·052	4·90	2·79	2·50	31·01

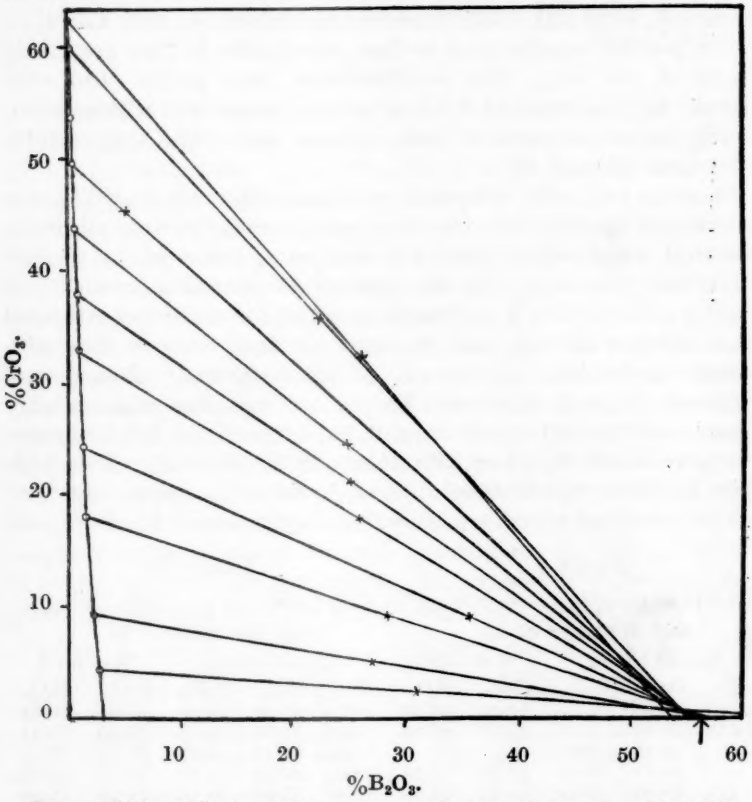
Table II.

Compositions (g. per 100 g.) and densities at 45°.

Liquid phase.			Wet solid.	
$d_4^{45°}$.	CrO_3.	B_2O_3.	CrO_3.	B_2O_3.
1·674	61·56	0·90	39·31	20·84
1·612	58·10	0·92	33·96	23·91
1·603	57·50	0·87	29·78	27·42
1·603	57·34	1·12	32·71	24·43
1·528	53·80	0·85	24·28	29·88
1·219	25·60	2·33	11·58	32·10
1·038	2·40	4·76	0·93	36·53

being calculated as B_2O_3; the data of Table I are also shown graphically in the figure, in which the value shown for the solubility of boron trioxide in water at 25° (3·1% B_2O_3) has been calculated from Seidell's tables. It will be observed that the productions of the tie-lines connecting liquids with corresponding wet solids pass very closely to the point representing the composition of boric

acid (56·3% B_2O_3, marked by an arrow on the diagram). The same occurs when the data for 45° are plotted. Apparent irregularities at 45° in the boron trioxide content of solutions containing much chromium trioxide may be ascribed to analytical errors, especially as the end-point in the total acidity determination is not sharp, and the small amounts of boron trioxide are determined by



The solubility of boric acid in aqueous solutions of chromic acid at 25°.

difference. For these reasons no great accuracy is claimed for the boron trioxide determinations, but from the behaviour of the tie-lines there seems no doubt that the solid phase is always boric acid. The shape of the curve appears to indicate that the depression of solubility of boric acid as the concentration of chromic acid is raised is due chiefly to common ion (hydrogen) action.

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CCV.—*The Dissociation Constants of Selenious Acid.*

By JAMES STUART WILLCOX and EDMUND BRYDGES RUDHALL PRIDEAUX.

THE first dissociation constant of selenious acid as determined by Ostwald ("Allgemeine Chemie," 1893) is $1{\cdot}59 \times 10^{-3}$ (conductivity method). The first and second constants as determined by Blanc (*J. Chim. phys.*, 1920, **18**, 39) are $2{\cdot}7 \times 10^{-3}$ and $5{\cdot}1 \times 10^{-8}$. Blanc, who stated his results with considerable reserve, appears to have used the following method. 0·595*N*-Sodium hydroxide was added, 0·1 c.c. at a time, to 0·0108*N*-selenious acid, and from the results obtained a conductivity–neutralisation curve was plotted, the rectilinear branches of which were produced in the usual manner to give the points of intersection corresponding to $NaHSeO_3$ and Na_2SeO_3. Solutions of the two salts prepared in accordance with these results were then treated with congo-red, phenolphthalein, or α-naphtholbenzoin and matched against buffer solutions of acetate and phosphate. These indicators were admittedly unsatisfactory; at the second point, $p_H = 9{\cdot}7$, phenolphthalein was at the limit of its change, and the colour change of naphtholbenzoin was not a pronounced one. Owing to the shape of the curve at these points, however, the accuracy in the determination of p_H was probably sufficient. We consider that a more serious source of error is the difficulty of finding the p_H points of inflection on the neutralisation–conductivity curve and of reproducing the correct stoicheiometrical proportions of acid and alkali with sufficient accuracy. For example, whilst 0·1 c.c. of alkali of the concentration employed by Blanc neutralises 6% of the acid, a change of 1% in the amount neutralised corresponds, from our curve, with a change of 1·0 in p_H value. We have therefore redetermined the constants with the aid of several indicators, including some of the modern ones, and at those stages of neutralisation at which the solutions are well buffered, and therefore not unduly sensitive to small errors in the addition of alkali.

EXPERIMENTAL.

A solution of selenium dioxide (prepared according to the usual method) in alcohol was filtered, and evaporated to dryness on the water-bath; the residue was recrystallised several times from hot water. To 20 c.c. of a 0·05*M*-solution of this selenious acid (factor 0·97, found by analysis, the acid being converted into and weighed as selenium) were added measured volumes of 0·189*N*-sodium hydroxide, free from carbonate, in the presence of suitable indicators. The colours were matched, in Nessler glasses, against

those of solutions obtained by the addition of the same alkali to 20 c.c. of the British Drug Houses universal indicator (J., 1924, **125**, 427) containing the same number of drops of indicator, and hence the hydrion concentrations corresponding to each 3% of acid neutralised were obtained.

Calculation of K_1 *and* K_2.—In the following tables x is the number of c.c. of alkali added to 20 c.c. of the selenious acid solution. The percentage of acid neutralised is calculated from the value of x, and the total concentration, c, of the acid is $0{\cdot}97/(20 + x)$. The concentration of the sodium salt, [NaHA], and of the anion derived from this, is $0{\cdot}189x/(20 + x)$. Individual values of h + [NaHA] and $c - (h$ + [NaHA]) introduced into the equation

$$K_1 = h(h + [\mathrm{NaHA}])/\{c - (h + [\mathrm{NaHA}])\} \quad . \quad . \quad (a)$$

give the values of K_1 up to $p_H = 3{\cdot}9$; the results marked * in the tables have been used. For values of p_H a little greater than 3 up to 4, equation (1) (J., 1924, **125**, 427), which does not take account of the total concentration, may be used, terms containing K_2 being omitted; *i.e.*,

$$K_1 = Rh/(1 - R) \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where R = equivalents of alkali added to 1 mol. of acid = % acid neutralised − 50. For values of p_H from 6·0 upwards, K_2 is calculated from the equation

$$K_2 = h(R - 1)/(2 - R) \quad . \quad . \quad . \quad . \quad (2)$$

The figures marked † in the tables have been introduced into equation (1), those marked ‡ into equation (2).

Thymol-blue.

x	0·5	1·0	1·5	2·0	2·55	3·0	3·57	4·0
% acid neutr.	5	9·8	14·5	19·5	24·9	29·2	35	39
p_H	2·2*	2·28*	2·35*	2·4*	2·45*	2·49*	2·65*	2·82*

In the following tables the percentage of acid neutralised is equal to $10x - 1$.

B.D.H. universal indicator.

x	= 4·7	5·0	5·1	5·2	5·3	5·4	5·5
p_H	= 3·45*	4·05†	4·7	5·45‡	6·3‡	6·8‡	7·15‡

Bromphenol-blue.

x	= 4·6	4·7	4·8	4·9	5·0	5·1
p_H	= 3·35*†	3·55*†	3·75*†	3·9*†	4·4	4·85

Congo-red.

x	= 4·6	4·7	4·8	4·9	5·0
p_H	= 3·25*	3·35*	3·63*	3·8*	4·2

Litmus.

x	= 5·2	5·4	5·5	5·6
p_H	= 5·9‡	6·4‡	6·55‡	6·98‡

Phenol-red.

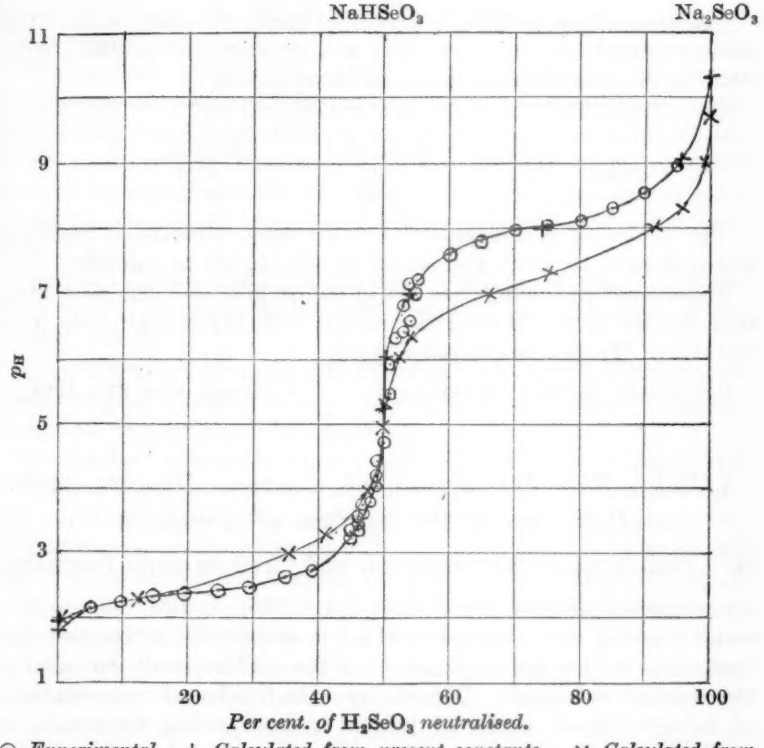
x	= 5·63	6·13	6·65	7·16	7·67
p_H	= 7·2‡	7·6‡	7·8‡	7·95‡	8·05‡

Thymol-blue.

x	= 8·18	8·69	9·2	9·71
% acid neut.	=80	85	90	95
p_H	= 8·1‡	8·3‡	8·55‡	8·95‡

FIG. 1.

The neutralisation of selenious acid.



⊙ *Experimental.* + *Calculated from present constants.* × *Calculated from Blanc's constants.*

The mean values of $10^3 \times K_1$ calculated from equations (*a*) and (1) above are: Thymol-blue, 4·18*; bromphenol-blue, 3·3*, 3·22†; congo-red, 4·32*; B.D.H. indicator, 4·37*†. Allowance being made for the number of observations, the general mean is: $K_1 = 4{\cdot}0 \times 10^{-3}$.

The mean values of $10^3 \times K_2$ are: B.D.H. indicator, 0·62;

litmus, 1·15; phenol-red, 0·72; thymol-blue, 1·04. The general mean is : $K_2 = 0{\cdot}87 \times 10^{-8}$.

A few values of p_H calculated from these constants are represented by + on the graph, *i.e.* :

% acid neut.	=	0	50	50·5	54·0	74·4	95·25	100
p_H	=	1·86	5·23	6	7	8	9	10·35

The experimental results are represented by circles, and the values calculated from Blanc's constants, at a molarity of 0·05, by ×.

% acid neut.	=	0	0·7	12·5	35·5	41·5	47·7	50·05	50·4
p_H	=	1·99	2	2·3	3·0	3·3	4·0	5	5·3
% acid neut.	=	52·4	54·6	66·5	75·25	91·5	95·5	99·05	
p_H	=	6·0	6·3	7·0	7·3	8·0	8·3	9·0	

The first branch of Blanc's curve lies distinctly above ours. The second branch of our curve has a very different position from Blanc's, the alkalinities throughout being greater.

The end-points in the titration of 0·05*N*-acid are :

	$NaHSeO_3$.	Na_2SeO_3.
Blanc	4·93	9·70
W. & P.	5·23	10·35

The choice of *p*-nitrophenol for the first titration is justified, and cochineal, lacmoid, and resazurin also should be suitable.

The second end-point does not of course give so accurate a titration, but we have obtained fair results with thymolphthalein (to a full blue). Tropæolin O is not so good.

UNIVERSITY COLLEGE, NOTTINGHAM. [*Received, April 27th,* 1925.]

CCVI.—*The Interaction of Carbon Dioxide and Hydrogen on the Surface of Tungsten.*

By CYRIL NORMAN HINSHELWOOD and CHARLES ROSS PRICHARD.

ACCORDING to Taylor (*Proc. Roy. Soc.*, 1925, *A*, **108**, 105), only a small fraction of a catalytic surface is necessarily active and this fraction is a function, not merely of the surface itself, but also of the reaction catalysed. This theory, which is based upon evidence of different kinds, was very helpful in interpreting the results of our investigation of the interaction of carbon dioxide and hydrogen on the surface of platinum, and other experiments (this vol., p. 806), where complete lack of correlation was sometimes found between total adsorption and that part of the adsorption which determines the kinetics of heterogeneous reactions. These all lend support to Taylor's view that catalysis may be confined to certain active centres.

In continuation, the interaction of carbon dioxide and hydrogen on the surface of tungsten has been investigated. Kinetically, the reaction is somewhat different from the reaction on the surface of platinum, but there is equally good evidence that it is determined by the adsorption of carbon dioxide and hydrogen on active centres. From measurements of the velocity of reaction, it must be inferred that saturation of the active surface with respect to each of the gases is reached without any appreciable displacement of the other. Saturation may be reached simultaneously and independently with respect to each. This seems to show that those centres which adsorb the carbon dioxide are not the same as those which adsorb the hydrogen, and that interaction requires the adsorption of molecules of each on adjacent centres of the appropriate kind.

The experimental method was essentially the same as that used in the previous investigation except that the reaction vessel was now a tungsten filament Osram lamp (30 volt, half-watt) to which were sealed capillaries leading to gas-holders, manometer and Gaede pump. The temperature of the filament was calculated from its resistance with the aid of Langmuir's data for the variation of the resistance of tungsten with temperature (*Physical Rev.*, 1916, **7**, 159).

The reaction was rendered irreversible by the absorption of the water formed in concentrated sulphuric acid in the bottom of the reaction vessel.

It was shown by analysis that under the conditions of the experiments the only reaction taking place to an appreciable extent was the simple change $H_2 + CO_2 = H_2O + CO$.

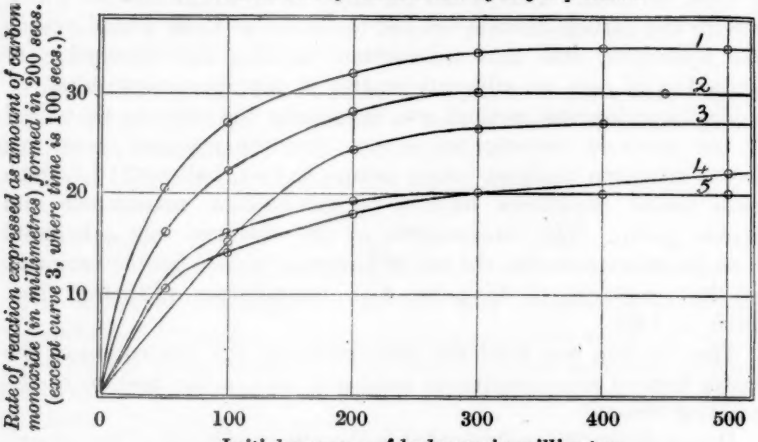
Pure carbon monoxide rapidly attacks a heated tungsten wire with formation of carbonyl, and the resistance of the wire increases very rapidly. Under the conditions of our experiments, however, the carbon monoxide produced in the reaction had no effect on the wire. Whether this was because the pressure was not great enough or because the other gases had a protecting action on the wire was not investigated, but it was ascertained with the greatest care that the resistance of the wire remained constant and, an even more delicate test, its catalytic activity remained remarkably steady. Control experiments under standard conditions were repeatedly made to ensure that the results were not being vitiated by any change in the wire.

Influence of the Pressure of the Hydrogen on the Rate of the Reaction.—Experiments were made with a constant pressure of carbon dioxide and varying hydrogen pressures. The rate of reaction first increases with the pressure of hydrogen and then remains constant, showing that the active part of the surface becomes saturated with hydrogen.

This is illustrated in Fig. 1. The curves were obtained with four different wires, the saturation capacities of which were naturally slightly different. The reaction–time curves are almost linear over a considerable range, so that the amount of carbon monoxide formed in 100 or 200 seconds is a quite legitimate and convenient measure of the initial rate of reaction. The following figures were obtained with one of the four wires used.

FIG. 1.

Relation between rate of reaction and hydrogen pressure.



(1) *Wire* 1, 50 *mm.* CO_2, 1182°; (2) *Wire* 3, 50 *mm.* CO_2, 1135°; (3) *Wire* 1, 100 *mm.* CO_2, 1182°; (4) *Wire* 5, 50 *mm.* CO_2, 1027°; (5) *Wire* 2, 50 *mm.* CO_2, 1215°.

TABLE I.

Influence of Hydrogen Pressure.

Pressure of carbon dioxide = 50 mm. in each case. Temperature = 1182°.

Press. of H_2 (mm.) $[H_2]$.	% CO_2 changed to CO in 100 sec.	200 sec.	300 sec.	Press. of H_2 (mm.) $[H_2]$.	% CO_2 changed to CO in 100 sec.	200 sec.	300 sec.
50	22	41	56	300	40	68	85
100	30	54	74	400	41	70	86
200	36	63	82	500	41	66	84

If σ is the fraction of the active surface covered with hydrogen, then the simplest type of adsorption equilibrium is expressed by $k_1(1 - \sigma)[H_2] = k_2\sigma$, whence $\sigma = [H_2]/(k_2/k_1 + [H_2])$.

Taking the readings at 100 seconds as proportional to initial velocities, a procedure justified by the almost linear form of the curves, and calling x the limiting rate at infinite hydrogen pressure,

we have for $[H_2] = 50$, $\sigma = 22/x$ and for $[H_2] = 100$, $\sigma = 30/x$; whence we find $x = 47$ and $\sigma = [H_2]/(57 + [H_2])$.

The following table gives the values of σ calculated from this equation, and also calculated on the supposition that the fraction of the active surface covered with hydrogen is given by the ratio of the actual velocity to the limiting velocity. This is referred to as $\sigma_{obs.}$

$[H_2]$	(50)	(100)	200	300
$\sigma_{obs.}$	(0·47)	(0·64)	0·77	0·85
$\sigma_{calc.}$	(0·47)	(0·64)	0·78	0·84

At 400 and 500 mm. $\sigma_{obs.}$ falls below the calculated value, that is to say, the rate of reaction does not increase quite as rapidly as it should. Indeed the calculated limiting rate is 47% of carbon dioxide transformed in 100 seconds, whilst the observed limiting rate is 41%. The hydrogen therefore has a certain displacing action on the carbon dioxide at higher pressures, but, as the table shows, this is negligible up to 300 mm. and even above this the displacing action is not wholesale as it would be if both gases competed for the same portions of the surface. Other wires gave similar results as the diagram shows, but detailed figures need not be given.

Influence of the Pressure of the Carbon Dioxide on the Rate of Reaction.—This is similar to that of the hydrogen pressure, but saturation is reached at lower pressures and a slight diminution in the rate of reaction occurs at the highest pressures. This indicates that the carbon dioxide can displace hydrogen to some slight extent, but the effect is almost negligible compared with that found when a platinum wire is used.

TABLE II.

Influence of Carbon Dioxide Pressure.

Pressure of hydrogen = 50 mm. in each case. Temperature = 1182°.

Press. of CO_2 (mm.) $[CO_2]$.	% total possible CO formed in 100 sec.	200 sec.	300 sec.	Press. of CO_2 (mm.) $[CO_2]$.	% total possible CO formed in 100 sec.	200 sec.	300 sec.
50	22	40	54	300	25	45	60
100	24	46	62	400	22	39	52
150	24	45	60	450	20	35	48
200	24	45	60	500	18·5	33·5	46

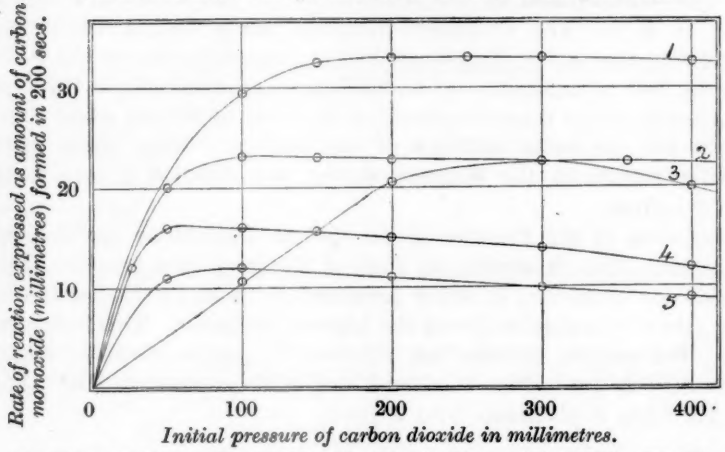
Taking the saturation value as 25 and ignoring the slight displacement effect at 400 and 500 mm., $\sigma_{CO_2} = [CO_2]/(5 + [CO_2])$ is found to represent the fraction of the active surface covered with carbon dioxide at various pressures.

Typical curves obtained with various wires are shown in Fig. 2.

The Kinetics of the Reaction.—We have seen that the surface can apparently become saturated with hydrogen and carbon dioxide independently. Thus, for example, the experiments in which the pressure of the carbon dioxide is varied show that the surface is nearly saturated with respect to this gas at 50 mm. pressure. Yet with 50 mm. of carbon dioxide the hydrogen pressure can be increased from 200 to 500 mm. with little change in the reaction rate. If hydrogen displaced carbon dioxide, the rate would pass through a pronounced maximum, as it does in the experiments where carbon dioxide displaces hydrogen from certain active points on platinum surfaces.

FIG. 2.

Relation between rate of reaction and carbon dioxide pressure.



(1) *Wire* 1, 100 *mm.* H_2, 1182°; (2) *Wire* 1, 50 *mm.* H_2, 1182°; (3) *Wire* 2, 100 *mm.* H_2, 1215°; (4) *Wire* 3, 50 *mm.* H_2, 1135°; (5) *Wire* 5, 50 *mm.* H_2, 1027°.

If we have nearly independent adsorptions in this way, the simplest assumption to make is that the rate of reaction is proportional to $\sigma_{H_2}\sigma_{CO_2}$.

From the results of the previous section we should therefore have

$$\text{Rate of reaction} = k \cdot \frac{[H_2]}{(57 + [H_2])} \cdot \frac{[CO_2]}{(5 + [CO_2])}.$$

The factors $[H_2]/(57 + [H_2])$ and $[CO_2]/(5 + [CO_2])$ were found from experiments with pressures of 50 mm. of carbon dioxide and hydrogen respectively. Using them, we may test the constancy of k at other pressures. The following are some typical experiments, all carried out at 1182°.

	Amount of carbon monoxide (mm.) formed in time t.			
t (seconds).	50 mm. H_2 } 50 mm. CO_2 }	100 mm. H_2 } 100 mm. CO_2 }	200 mm. H_2 } 200 mm. CO_2 }	300 mm. H_2 } 300 mm. CO_2 }
100	11·5	18·5	23	29
200	20	34	46	58
300	27	46	64	87
400	32	56	87	116
500	36·5	—	105	—
	$k = 27$	$k = 30$	$k = 30$	$k = 35$

The following table gives values of k for a number of similar experiments. In every case the rate of reaction from which k is obtained is expressed as the amount of carbon monoxide produced in 100 seconds. All the figures refer to wire 1.

Press. of CO_2 (mm.).	Press. of H_2 (mm.).	k.	Press. of CO_2 (mm.).	Press. of H_2 (mm.).	k.
50	100	26	100	50	25·5
100	100	25	100	100	25
150	100	27·5	100	150	27
200	100	27·5	100	200	31·5
300	100	27	100	300	31
500	100	27			

The idea of independent adsorption of the two reacting substances thus seems to be substantiated.

The Influence of Temperature.—The temperature coefficient of the reaction rate was measured with one only of the wires. Experiments were made with a standard mixture of hydrogen (100 mm.) and carbon dioxide (100 mm.) at each temperature.

CO (pressure in mm.) formed in	Temperature.				
	953°.	1061°.	1135°.	1231°.	1303°.
100 secs.	2	5·5	11	21	29
200 „	4	11	22	38	51
300 „	7	16	33	52	—

The value of the apparent heat of activation calculated from these by means of the Arrhenius formula is 30,000 calories.

Summary.

The rate of the reaction $H_2 + CO_2 = H_2O + CO$ on the surface of a tungsten filament heated to temperatures between 1000° and 1300° is proportional to $\sigma_{H_2} \cdot \sigma_{CO_2}$, where σ_{H_2} and σ_{CO_2} are the fractions of certain active parts of the surface which are covered with adsorbed hydrogen and carbon dioxide respectively.

The adsorption of each gas on the active centres is almost independent of the pressure of the other. This shows that the whole surface is not active, but that only certain parts are able to adsorb hydrogen and carbon dioxide and cause them to react. The parts which adsorb hydrogen in this way are different from those which

adsorb and render reactive the carbon dioxide. Interaction apparently takes place when molecules of the two gases are adsorbed on adjacent centres of the appropriate kind.

We are indebted to the Royal Society and to the Chemical Society for grants with which some of the apparatus used was purchased.

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CCVII.—*The Relation of Homogeneous to Catalysed Reactions. The Catalytic Decomposition of Hydrogen Iodide on the Surface of Gold.*

By CYRIL NORMAN HINSHELWOOD and CHARLES ROSS PRICHARD.

A HETEROGENEOUS catalyst may influence a reaction in two ways. It may modify the mechanism of the chemical change by allowing it to proceed along another path. It may also facilitate the transformation by lowering the energy of activation, *i.e.* the energy which must be imparted to the reacting molecules before they can be transformed chemically. There is very good evidence that in homogeneous chemical changes this energy of activation is the quantity which plays the decisive part in determining the rate at which the reaction can take place at a given temperature. It must therefore be expected to have considerable significance in catalytic reactions also.

The modification of reaction mechanisms is exemplified by the thermal decomposition of nitrous oxide. The homogeneous reaction is bimolecular (*Proc. Roy. Soc.*, 1924, *A*, **106**, 284). On the surface of platinum or gold the change becomes unimolecular (*Proc. Roy. Soc.*, 1925, *A*, **108**, 211; this vol., p. 327). It is resolved into the stages $N_2O = N_2 + O$ and $O + O = O_2$. The affinity of the metals for atomic oxygen renders possible the first stage, which could only take place homogeneously if a very large amount of energy were communicated to the nitrous oxide molecule, for the production of free oxygen atoms is a highly endothermic process. The metal acts as a resting place for the oxygen atoms until they meet others of their kind. It appears also that on the surface of platinum ammonia decomposes unimolecularly (this vol., p. 1105), whilst, although the homogeneous reaction has not been actually observed, it is almost certain from analogy with known examples that it would be bimolecular.

The question of the influence of the second factor, the lowering of the energy of activation, has not received a conclusive answer. The nitrous oxide decomposition is the only example hitherto investigated in which a homogeneous reaction has been quantitatively compared with the corresponding heterogeneous change on one or more surfaces. The homogeneous transformation requires the collision of two molecules possessing a combined energy of 58,500 calories. This quantity can be obtained from the temperature coefficient of the reaction velocity. The corresponding heats of activation obtained in the same way from the temperature coefficients of the surface reactions on gold and platinum are 29,000 and 32,500 calories, respectively. But it is not quite justifiable to compare these various values directly. In the case of bimolecular homogeneous reactions, there is ample evidence that the heat of activation is a real measure of the energy that the colliding molecules must possess in order that they may be transformed (compare J., 1924, **125**, 1841). In heterogeneous reactions, however, the temperature coefficient of the reaction velocity depends partly on the variation with temperature of the amount of reactant actually adsorbed on the surface, and therefore the value of E obtained from the formula $d \log k/dT = E/RT^2$ requires correction before it represents the energy which the adsorbed molecules must acquire in order to undergo chemical change (compare J., 1923, **123**, 1014). There exists a real temperature coefficient of the rate of reaction of the molecules actually adsorbed. This would furnish a true value for the heat of activation having direct physical meaning, but since the relative numbers of molecules of reactant adsorbed at different temperatures are not known, the correction which would make the observed reaction velocities at various temperatures directly comparable with one another cannot be applied. The adsorption of the reacting gas diminishes with temperature. This acts in opposition to the normal increase of the true reaction rate with temperature and thus the observed temperature coefficient is less than the true value. Thus $E_{obs.}$ is too small. It is likely that the necessary correction is quite small compared with 30,000 calories, so that we are probably safe in concluding that the total activation required in each of the surface reactions of the nitrous oxide is much less than in the homogeneous reaction. It is true that the 58,500 calories refers to 2 gram-molecules, whilst the values 29,000 and 32,500 refer to 1 molecule only, the catalytic reactions being unimolecular. But the fact remains that the total activation necessary in the surface reaction is very much less, since in the homogeneous reaction one molecule is not activated without the other.

These conclusions are interesting, but not free from a little uncertainty, arising from the lack of knowledge about the exact correction that should be applied to the experimentally found heats of activation in the surface reactions. The object of this paper is to present results which are free from any such uncertainty.

The difficulty to be overcome is the unknown variation in the degree of adsorption of the reacting substance at different temperatures. The difficulty vanishes in one special case, namely, when the surface is saturated at all temperatures so that the number of molecules present is always the same. This state of affairs is recognised by the fact that the absolute rate of reaction becomes independent of the pressure of the reacting gas, or, in other words, the reaction is of zero order.

The heterogeneous decomposition of ammonia on the surface of tungsten was recently found to be approximately of zero order (this vol., p. 1105) and results are described in the present paper to show that the decomposition of hydrogen iodide on the surface of gold is also of this type. The observed heats of activation in these reactions are therefore equal to the true values and may be compared directly with the values for the corresponding homogeneous reactions.

The value found for the decomposition of hydrogen iodide on the surface of gold is 25,000 calories. Since the reaction is of zero order, it is impossible to tell whether one or two molecules of hydrogen iodide are involved in it; to decide this point is only possible with sparsely covered surfaces—when the surface is saturated, it makes no difference to the actual kinetics of the reaction whether one molecule decomposes spontaneously or two adjacent ones interact. From analogy with the case of nitrous oxide, it seems probable that only one is involved. However this may be, the total heat of activation is again very much lower than that of the homogeneous reaction, which amounts to 44,000 calories.

With regard to ammonia the homogeneous reaction has not been observed, but its velocity has been shown to be negligible up to 1050° (this vol., p. 1105). From analogy with the decompositions of ozone, chlorine monoxide, hydrogen iodide, and nitrous oxide, it seems certain that it would be found to be bimolecular, and from the table given by Hinshelwood and Hughes (J., 1924, **125**, 1841), showing the relation between the heat of activation of bimolecular reactions and the temperatures at which they attain a given rate, it is obvious that the heat of activation in the homogeneous ammonia decomposition cannot be less than about 80,000 calories. The heat of activation of the reaction on the surface of tungsten was found to be 38,700 calories.

The following table gives a summary of the various relationships :

Reaction. Thermal decomposition of	Total activation required for the homogeneous change (bimolecular).	Total activation required for the heterogeneous change (probably or certainly unimolecular).
Hydrogen iodide	44,000	25,000 (gold)
Nitrous oxide	58,500	29,000 * (gold)
		32,500 * (platinum)
Ammonia	probably >80,000	39,000 (tungsten)

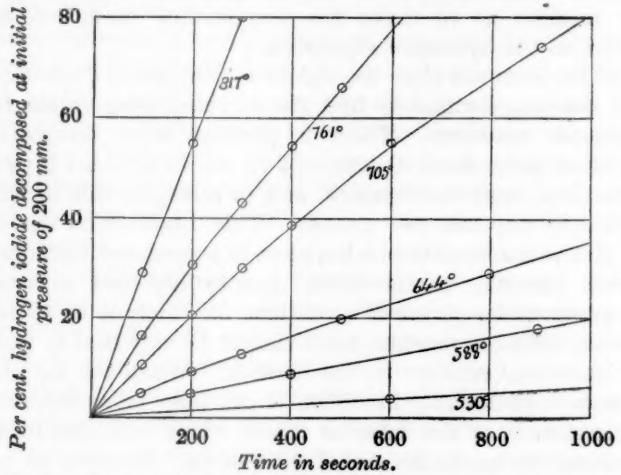
* + small correction ?

(The decomposition of ammonia on platinum cannot be brought into this table because it is retarded by the hydrogen formed in such a manner as to make the temperature coefficient mainly a function of the hydrogen adsorption.)

It will be observed that the values for the surface reactions are in each case approximately half the corresponding values for the homogeneous reactions. There is perhaps some temptation to suppose that the numerical ratio of 2 : 1 would be exact if perfectly accurate data could be obtained, and to interpret this in terms of activation by one and two quanta. This, however, is not admissible. Activation doubtless takes place in accordance with quantum dynamics, but the characteristic quanta involved in reactions taking place under physical conditions so different as to lead to completely different reaction rates cannot be expected to bear any simple numerical relation to one another. When the stability of a molecule is profoundly modified, it can only be as the result of a rearrangement of the internal forces which will also lead to a fundamental change in the size of the quanta. We must at present content ourselves with observing the greatly decreased heat of activation in the surface reactions and the probable change from bimolecular to unimolecular processes.

The Catalytic Decomposition of Hydrogen Iodide on Gold.—The experimental procedure for measuring the rate of decomposition of hydrogen iodide on the surface of a heated gold wire was exactly as described in previous papers (this vol., p. 327; *Proc. Roy. Soc.*, 1925, *A*, **108**, 211). The iodine liberated in the reaction was condensed on the walls of the vessel, which was kept at 0°. The vapour pressure of iodine at 0° is negligible. The reaction $2HI = H_2 + I_2$ is therefore accompanied by a decrease in pressure which allows its rate to be measured. There existed the possibility that the gold wire might be attacked by the iodine. Gold iodide is, however, decomposed at 200°, and the lowest temperature of the wire in the experiments was 530°. Iodine, therefore, under the experimental conditions never had the opportunity of reaching

the wire except at a temperature several hundred degrees above that at which gold iodide ceases to be capable of existence. It should be mentioned that gold iodide is apparently endothermic, although F. Meyer finds that the interaction of gold and iodine diminishes with temperature and almost ceases above 190°. This leaves it just possible that there might be slight interaction again at higher temperatures. But it is in the highest degree unlikely that the dissociation pressure of gold iodide would at 800° have fallen below the minute iodine pressure prevailing in these experiments, and the special experiments made to test for interaction showed that it was in fact inappreciable. The change in pressure observed when the decomposition was complete coincided with the



Catalytic decomposition of hydrogen iodide with surface of gold. Initial pressure 200 mm.

theoretical value. The resistance of the wire at 0° was measured from time to time and found not to vary as it would if the gold were being attacked, and the catalytic activity remained constant. The action of the gold may therefore be regarded as purely catalytic in the usual sense of the term.

The hydrogen iodide was prepared by dropping syrupy phosphoric acid on a mixture of finely divided potassium iodide and phosphorus pentoxide in an apparatus made entirely of glass. The gas was dried by passage over phosphorus pentoxide and condensed in a bulb surrounded by liquid air. While the hydrogen iodide was kept solid, any non-condensible impurities such as hydrogen were pumped away. About one-third of the liquid was then allowed to distil into an evacuated blackened glass bulb, provided with a tap. This bulb was then sealed to the decomposition apparatus.

Since hydrogen iodide attacks mercury, special precautions have to be taken in measuring the reaction velocity with the aid of a mercury manometer. Fortunately, it was found that hydrogen has no influence on the velocity of decomposition and it was therefore convenient to allow the reaction always to proceed in the presence of a certain amount of hydrogen, which was let into the apparatus first and thus acted as a buffer in the capillary manometer, protecting the mercury completely from any attack by the hydrogen iodide.

The following figures show that hydrogen has no effect on the reaction velocity.

Temp. 705°. HI alone (200 mm.). Amt. decomposed in 200 secs. = 32 mm. HI (200 mm.), H_2 (100 mm.). Amt. decomposed in 200 secs. = 34 mm.

Temperature 705°.

Time (sec.).	Amount of hydrogen iodide decomposed (mm.). 50 mm. H_2 / 100 mm. HI	100 mm. H_2 / 100 mm. HI	200 mm. H_2 / 100 mm. HI
100	19	18	18
200	35	36	34
300	49	50	47
400	61	62	59
500	72	72	68

The absolute amount of hydrogen iodide decomposed in unit time is nearly independent of its pressure. This may be seen by an inspection of the following results. It will also be observed that the curves shown in the figure are not far from linear.

Temperature 705°. 100 Mm. of hydrogen present in each expt.

Time (sec.).	Amount of hydrogen iodide decomposed. 100 mm. HI.		200 mm. HI.	400 mm. HI.	Time (sec.).	Amount of hydrogen iodide decomposed. 100 mm. HI.		200 mm. HI.	400 mm. HI.
100	18	18	22	26	800	88	90	—	—
200	34	36	42	46	900	—	—	148	174
300	48	50	60	—	1200	—	—	—	224
400	60	62	76	76	1500	—	—	—	266
500	69	72	—	—	1800	—	—	—	308
600	77	79	110	118	2100	—	—	—	334
700	—	—	—	—	2400	—	—	—	352

Temperature 588°.

Time (secs.).	Amount of hydrogen iodide decomposed. 200 mm. HI.	400 mm. HI.
200	10	11
400	18	—
500	—	26
900	36	44
1600	54	—

Temperature 817°.

Time (secs.).	Amount of hydrogen iodide decomposed. 100 mm. HI.	200 mm. HI.	400 mm. HI.
100	58	58	76
200	84	111	144
300	92	162	196
400	—	—	252
500	—	—	298
600	—	—	334
700	—	—	354

The reaction is thus nearly of zero order, a fourfold increase in pressure increasing the absolute reaction rate only in the ratio 1 : 1·45 at 705° and 1 : 1·46 at 817° instead of in the ratio 1 : 4·0, as would happen if the change were according to the unimolecular law.

The nearness of this ratio to unity shows that saturation of the surface is nearly reached at both temperatures and the equality of the ratio at the two temperatures shows that the deviation from saturation at a given pressure cannot differ appreciably in the two cases. The temperature coefficient should therefore be independent of the variation of adsorption with temperature.

The influence of temperature on the velocity of reaction was measured from 530° to 817°. From the slope of the line obtained by plotting the reciprocal of the absolute temperature against log t, where t is the time taken for 50 mm. out of an initial 200 mm. of hydrogen iodide to decompose, a value of 25,000 calories is found for the heat of activation. The same value is found from the times required for 20 mm. out of the initial 200 mm. to react.

Absolute temperature.....	803°	861°	917°	978°	1034°	1090°
t (seconds)	6000	1450	650	242	157	85

A discussion of these results has been given in the earlier part of the paper.

Summary and General Conclusions.

It is shown that the thermal decomposition of hydrogen iodide on the surface of a heated gold wire is a catalytic reaction the rate of which is almost independent of the pressure of the gas and uninfluenced by the presence of hydrogen.

It is pointed out that such " zero-order " reactions are of special importance because their temperature coefficients are not influenced by the changing degree of adsorption of the reactant. The " heat of activation " may therefore be expected to have, without correction, the direct physical significance that it possesses in the case of homogeneous reactions.

On the basis of the results described in this and previous papers it is now possible to make a comparison between the mechanism of homogeneous reactions and that of the corresponding reactions catalysed by surfaces.

The reactions considered are the homogeneous thermal decomposition of nitrous oxide, hydrogen iodide, and ammonia, and the heterogeneous decomposition of nitrous oxide on platinum and gold, of hydrogen iodide on gold, and of ammonia on tungsten.

It is shown that the surface reactions have heats of activation only about half as great as those of the bimolecular homogeneous changes. But the surface reactions have been shown in some cases

to involve only one molecule, and this is probably the general rule. Thus the function of the surfaces in the reactions considered is to permit the occurrence of a unimolecular process instead of a bimolecular process requiring an energy of activation about twice as great.

We are indebted to the Royal Society and to the Chemical Society for grants in aid of this work.

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CCVIII.—*The Adsorption of Water from the Gas Phase on Plane Surfaces of Glass and Platinum.*

By IVAN ROY MCHAFFIE and SAM LENHER.

THE results of numerous investigators (Ihmori, *Ann. Phys. Chem.*, 1887, **31**, 1006; Briggs, *J. Physical Chem.*, 1905, **9**, 617; Trouton, *Proc. Roy. Soc.*, 1907, *A*, **79**, 383; Katz, *Proc. K. Akad. Wetensch. Amsterdam*, 1912, **15**, 445; Parks, *Phil. Mag.*, 1903, **6**, 517) would indicate that the film of water adsorbed on a glass surface at the ordinary temperature from the gas phase may be of more than monomolecular thickness when the pressure of water vapour is not far removed from the saturation value at the corresponding temperature. Langmuir (*Proc. Faraday Soc.*, 1922, 607; *Physical Rev.*, 1915, **6**, 79), in stating his important theory of adsorption, says, "Only when we have saturated vapours should we ever get films of gas molecules of more than monomolecular thickness." The present research is a study of the films of water adsorbed from the gas phase on plane glass and platinum surfaces when the pressure of the water vapour is near the saturation value.

The method employed is such that a direct measurement of the number of molecules adsorbed from a saturated vapour on a known area of a plane surface can be made. The phenomenon on which this study of adsorption is based was observed by one of us in another research and may be briefly stated as follows. Consider a closed, evacuated system into which a limited mass of water is introduced. This mass must be such that at some higher temperature the entire amount will be in the state of vapour, but at the initial temperature part of the water exists in the liquid phase, the remainder being in the gas phase. The pressure in the system due to water vapour should be equal to the vapour pressure of water at the initial tem-

perature, and the pressure at successively increasing temperatures should be equal to the vapour pressure of water at the corresponding temperatures until all of the water present has passed into the gaseous phase.

The increases of pressure above this value due to increasing temperatures should be proportional to the absolute temperature. If the temperatures be plotted as abscissæ and the corresponding pressures as ordinates, the curve obtained from these theoretical considerations would be *aob* (Fig. 2). The portion *ao* is the vapour-pressure curve for water and *ob* is the curve showing the effect of temperature on the pressure of a gas at constant volume. The values of pressure in the system as a function of temperature, determined experimentally, do not agree with these theoretical considerations. The experimental curve for such a system is *acb* (Fig. 2). At temperatures below the point *a* the experimental curve coincides with the vapour-pressure curve for water (*ao*), and at the temperatures above the point *b* the experimental curve coincides with the theoretical curve *ob*. The measurements of pressure at temperatures between *a* and *b* are in every case less than those expected from the simple theory given above. The greatest deviation of the experimental curve from the theoretical curve is at the temperature given graphically by the point *o*. At this temperature all the water in the system should be in the gaseous phase, if adsorption did not occur, and the pressure due to water vapour should be equal to the vapour pressure of water at this temperature. If the temperature and the pressure of the system are those of the point *b*, then all of the water present exists in the gaseous phase. The pressures determined experimentally at successively decreasing temperatures between *b* and *o* should be those represented by the line *bo*, if adsorption did not occur, but the values of pressure determined lie along the curve *bc*; continued pressure measurements at temperatures between *c* and *a* give the curve *ca*, the experimental curve from *a* to *b* being a smooth continuous curve.

The pressure measured at any temperature between *a* and *b* is less than the expected value. This decrease of pressure must be due to adsorption of water from the gas phase. That equilibrium is established along the curve is evident from the fact that at any one temperature the value of the pressure measured is the same whether the system be heated to that temperature or cooled down from a higher one.

It is not possible to state definitely from the findings of this research whether the adsorption measured takes place directly on the solid surface of the glass or platinum, or on the surface of a stable adsorbed layer of water which is on the surface throughout

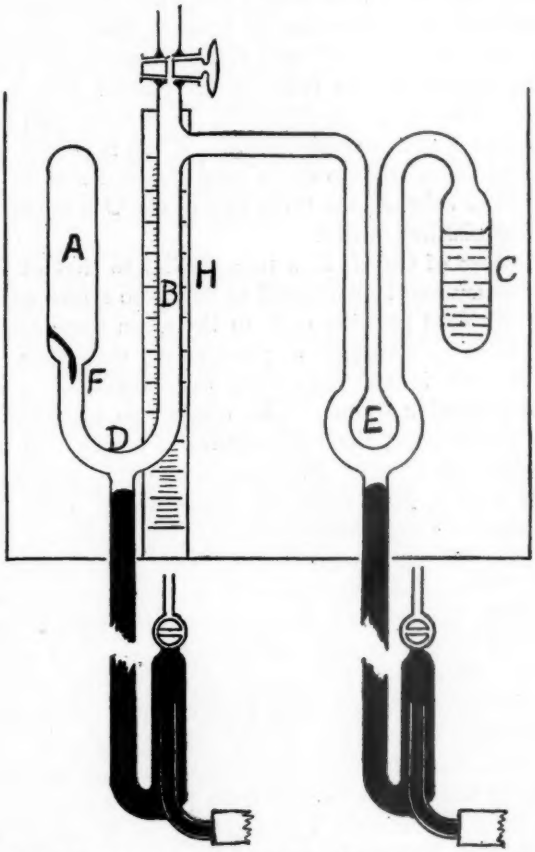
all of the experiments. The procedure adopted is such that this question cannot be settled here.*

The method of experimentation was as follows.

The Adsorption of Water on a Glass Surface.

The Apparatus.—A diagram of the apparatus employed to measure the pressures in a constant-volume system is shown in Fig. 1.

FIG. 1.



A is a hollow cylindrical tube of soft Duroglass closed at the top end; the lower end is sealed to a glass tube of smaller diameter

* The adsorbing surfaces in the case of glass or platinum (the materials employed in this investigation) are not of course ideally plane as assumed in this paper, and so the amount of substance adsorbed per unit of area of adsorbing surface may be smaller than as calculated. A discussion of this question is reserved for a subsequent paper.

which is bent into a U, D. At the bottom of the U a glass tube 78 cm. long is sealed; a mercury air-trap is sealed to the bottom end of this tube, which is in turn attached to a mercury reservoir by means of rubber tubing. The internal dimensions of A were carefully measured before the tube was constructed; tubing of uniform bore and as free as possible from imperfections was chosen. The tube was annealed for 4 hours at 500°. The internal surface of the tube A was cleaned by first washing with organic solvents. The tube was then filled with freshly prepared chromic acid cleaning solution and allowed to stand for 24 hours. The cleaning was completed with fuming nitric acid and repeated washings with distilled water. The volume of the tube to the pointer F was calibrated to 0·005 c.c. The open end of the U, D, is connected to mercury diffusion pumps and a McLeod gauge. A tap is placed in the tube B. A few cm. below the tap a side tube is sealed making connexion with a second U tube, E, the other end of the U is sealed to a bulb, C, containing distilled water.

To the bottom of the U, E, a tube similar to that at the bottom end of D is sealed and is connected as before to a mercury reservoir. In making the final position seals in the clean apparatus the glass blowing was done through a phosphorus pentoxide tube. All the mercury used in the apparatus was thoroughly purified and dried by the usual methods. The whole was mounted vertically in a water thermostat, the temperature of which was maintained and controlled electrically, the thermoregulator permitting of an adjustment over a long range of temperature. The tubes from D and E passed through stuffing boxes in the bottom of the thermostat. A scale, H, calibrated to 0·01 mm., was mounted behind the tube B. Plate glass windows were set in the sides of the thermostat so that the differences in level between the mercury in F and B might be read by means of a cathetometer provided with a micrometer screw adjustment. Evacuation was carried out by means of a diffusion pump backed by a Töpler pump. Pressure readings at high vacuum were made by the McLeod gauge. Before the apparatus was used for any determinations the air was entirely removed from the apparatus and from the water in C.

Experimental Procedure.—The mercury in D and E is lowered and the pressure of the air reduced by means of the water pump to such a value that the water in C just begins to boil. Excessive boiling must be avoided, otherwise water will be carried over from C into the U, E. The mercury is then raised in E and the evacuation continued by the diffusion pump until the pressure remaining in the apparatus cannot be read on the McLeod gauge. The tap B is then closed and the mercury lowered in E.

When sufficient time has elapsed for the pressure to come to equilibrium with the vapour pressure of the water in C, the mercury in E is again raised and evacuation continued. This process is carried out a sufficient number of times so that the last remaining traces of air in C are removed. The position of the pointer F is now determined relative to the scale H.

When the vacuum is as high as possible, the mercury in D is raised until the tip of the pointer just touches its reflected image in the mercury meniscus. The position of the meniscus in B is then read off to 0·01 mm. on the scale H. This determination of the "zero" position of the pointer was carried out a number of times and in every case concordant results were obtained. The tap B is then closed and the mercury lowered in D and E. The temperature of the thermostat is adjusted so that the value of the pressure in A due to water vapour, and hence the mass of water in A, is that desired for a particular measurement. During the filling process the mercury in D and E is lowered just below the bottom of the U's so that any condensation of water on the mercury surfaces is avoided. The mercury is then raised in D and E, B is opened, and the apparatus completely evacuated to the mercury surfaces. The pressure in A is then determined by raising the mercury in D until the tip of the pointer just touches its reflected image, and reading off with the cathetometer the position of the meniscus in B on the scale H. The difference between this value and that of the "zero" position of the pointer is the pressure in mm. of mercury at the temperature of the thermostat exerted by the water vapour in A. From this reading it is possible to decide whether or not the desired amount of water has been admitted to A. If it is not sufficient, the temperature of the thermostat is increased, and the filling operation again performed. If too much water has been admitted, B is closed, the mercury is lowered in D, permitting some of the water vapour to escape into B, the mercury is then raised in D, the tap B is opened, and the portion of the apparatus above the mercury surfaces is further evacuated. This procedure is continued until the amount of water in A is that desired. It is not essential at this stage to know exactly the mass of water which has been admitted to A, since the mass may be determined from later measurements. Readings of the pressure in A are made both at successively increasing and decreasing temperatures, and in both instances readings obtained at any one temperature agree to 0·01 mm. The temperature is increased until the water vapour is behaving as a gas whose pressure at constant volume is increasing linearly with increasing temperature. The readings are continued at successively lower temperatures until the pressures measured agree as nearly

as possible with the vapour pressures of water at the corresponding temperatures.

Results.—The readings obtained in a series of measurements are given in Table I. T is the absolute temperature, and p the pressure read at the corresponding temperature in mm. of mercury at 0·0° C. The volume of the tube A was 13·307 c.c. and the area of the internal surface was 55·10 sq. cm.

TABLE I.

$T°$ abs.	p mm.	N/cm.² $\times 10^{-14}$.	θ.	$-\Delta F$.	$T°$ abs.	p mm.	N/cm.² $\times 10^{-14}$.	θ.	$-\Delta F$
		No. 1.					No. 2.		
293·0	16·90	1052·0	88·5	20·6	289·0	13·25	1387·0	117·0	—
298·0	22·73	616·4	51·8	26·1	293·0	16·92	1109·0	93·2	20·4
302·0	27·54	267·2	22·5	52·2	296·0	20·46	841·3	78·0	22·5
305·0	29·71	119·5	10·5	110·4	298·0	22·80	652·7	56·1	24·3
308·0	30·65	70·3	5·9	194·8	300·0	25·27	487·7	41·0	33·6
311·0	31·44	32·8	2·7	282·2	303·0	28·96	231·3	20·0	60·7
314·0	31·97	16·4	1·4	374·1	306·0	30·82	98·4	8·3	152·0
317·0	32·40	7·03	0·6	468·2	308·0	31·47	65·6	5·5	178·6
320·0	32·80	—	—	—	311·0	32·26	30·5	2·5	260·2
323·0	33·23	—	—	—	314·0	32·91	4·7	0·4	356·1
					317·0	33·31	—	—	—
					320·0	33·83	—	—	—
					323·0	34·19	—	—	—
		No. 3.					No. 4.		
293·0	16·99	1444·0	121·0	14·3	298·0	23·76	2188·0	184·0	0·0
298·0	23·08	986·6	83·0	17·1	301·0	27·85	1638·0	137·7	10·7
301·0	26·90	707·8	59·5	19·5	304·0	32·96	1265·0	106·0	13·3
304·0	31·06	407·7	34·0	49·1	307·0	37·85	918·8	77·2	32·2
307·0	34·26	185·1	15·5	92·7	310·0	43·07	550·8	46·3	54·5
310·0	35·92	86·7	7·2	165·7	313·0	47·02	286·0	24·0	98·6
313·0	37·05	25·8	2·1	248·5	316·0	48·70	194·5	16·3	179·1
316·0	37·79	—	—	—	319·0	51·55	21·1	1·4	237·4
					322·0	52·32	—	—	—
					325·0	53·11	—	—	—
					328·0	53·75	—	—	—

In Fig. 2 the values of T given in Table I are plotted as abscissæ and the corresponding values of p as ordinates. The vapour-pressure curve for water is also given, plotted from the data of Scheel and Heuse (*Ann. Phys.*, 1910, **31**, 715).

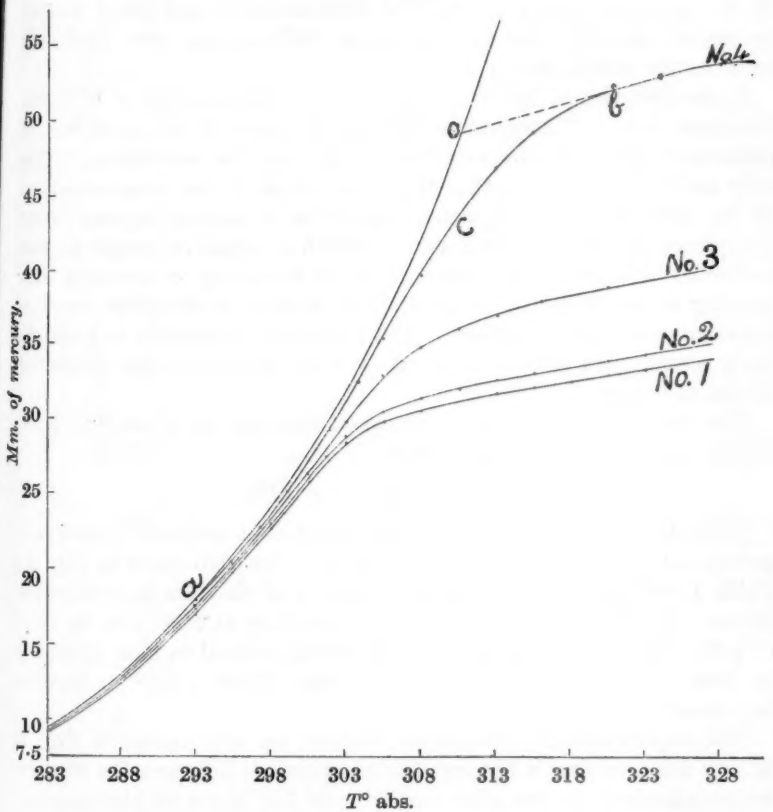
At the higher temperatures the values of p are increasing linearly with increasing temperature. The mean value of the rate of increase per degree is 0·0037. This is sufficiently near the temperature coefficient of a perfect gas that water vapour at these concentrations may be considered to behave as such. Hence the mass of water present in the system may be calculated from the equation $pv = nRT$, where p is the pressure at some point on the linear portion of the experimental curve at the temperature $T°$; v is the volume of the system; n is the number of moles present; and R is the gas constant, which, if p is measured in mm., is equal to 6·244 ×

10^4 c.c.-mm. per degree. If any other point be chosen on the experimental curve, then the temperature and pressure will be T_1 and p_1. The number of moles of water in the gaseous phase can be calculated at the new temperature and pressure and is given by $n_1 = p_1 v/RT_1$.

The number of moles adsorbed on the glass surface will be $n - n_1$, where $n - n_1 = pv/RT - p_1 v/RT_1$.

FIG. 2.

Glass–water.



The Avogadro number is $6{\cdot}06 \times 10^{23}$. The actual number of molecules adsorbed on the glass surface is $(n - n_1) \times 6{\cdot}06 \times 10^{23}$, or, if this number be denoted by N, then

$$N = \frac{v}{R}\left(\frac{p}{T} - \frac{p_1}{T_1}\right) \times 6{\cdot}06 \times 10^{23}.$$

Since v, the volume of the apparatus, and R are constant,

$$N = (p/T - p_1/T_1) \times 1{\cdot}292 \times 10^{20}.$$

The area of the inside surface of the glass tube can be calculated to 0·05 sq. cm. In this calculation, the area of the glass pointer must be included. The value obtained was 55·10 sq. cm. The number of molecules adsorbed per sq. cm. (N/cm.^{2}) is given by,

$$N/\text{cm.}^2 = (p/T - p_1/T_1) \times 2{\cdot}344 \times 10^{18}.$$

The degree of accuracy of this calculation is fairly high. The temperature was read to 0·05°; the pressure to 0·01 mm.; the volume was calibrated to 0·005 c.c., and the area calculated to 0·05 sq. cm. If the equation giving N/cm.^{2} be differentiated and these values be substituted for the corresponding differentials, the probable error in the calculation is 0·50%.

If the diameter of the water molecule be taken as $2{\cdot}9 \times 10^{-8}$ cm. (compare Jeans, "Dynamical Theory of Gases"), the number of molecular layers in the adsorbed layer may be calculated. The only assumption made, other than that made in the determination of the diameter, is that each molecule in a monomolecular layer occupies a square area each side of which is equal in length to the molecular diameter. No assumption is necessary concerning the packing of one layer on another. The surface of the glass may be considered as a plane surface. The number of molecules in a single layer covering an area of 1 sq. cm. is $1/d^2$, where d is the diameter of the molecule.

The number of layers in an adsorbed film will be $N/\text{cm.}^2 \div 1/d^2$. If this value be denoted by θ, then

$$\theta = (p/T - p_1/T_1) \times 1972.$$

Table I, column 3, gives the total number of molecules adsorbed per sq. cm. (N/cm.^{2}) at the temperatures $T°$ for each curve in Fig. 2; Table I, column 4, gives the thickness, θ, of the film in molecular layers. In Table I, No. 4, the initial reading at 298° abs. is that of a film the equilibrium pressure of which is equal to that of water in bulk. Such a film is produced when 2188×10^{14} molecules are adsorbed per sq. cm.

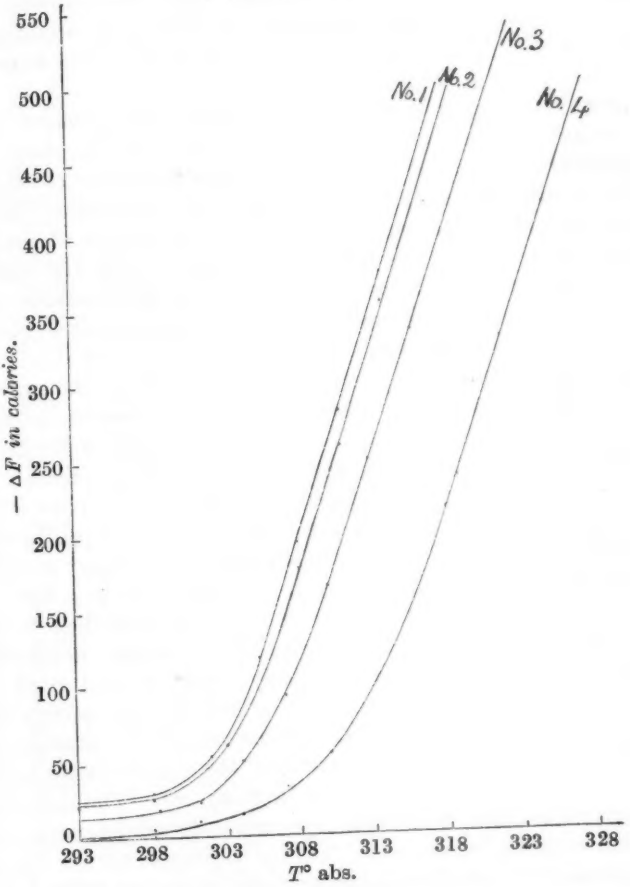
The experimentally measured pressure on any curve in Fig. 2 at any temperature is the equilibrium pressure between the film of water adsorbed on the glass surface and the water in the gaseous phase in the system. Taking as a standard state that of saturated water vapour at each temperature, it is possible to calculate from the experimental data the decrease of free energy, $-\Delta F$, corresponding to the adsorbed film. These values of $-\Delta F$ are calculated from the well-known thermodynamic equation, $-\Delta F = RT \log (p/p_1)$, where p is the vapour pressure of water at $T°$, p_1 is the equilibrium pressure of the adsorbed film at the same temperature, and R is the gas constant in calories per degree. The values of

$-\Delta F$ in calories per mol. of water adsorbed are given, together with the corresponding temperatures and thicknesses of film, in Table I.

The changes of free energy are shown graphically as a function of temperature in Fig. 3. It is evident from these curves that the

FIG. 3.

Glass–water.



free energy change accompanying the adsorption of water on glass is increasingly less for each new layer adsorbed.

Further discussion of these results will be more fruitful after the results for the adsorption of water on platinum have been given.

The Adsorption of Water on a Platinum Surface.

By a modification of the apparatus, as shown in Fig. 1, the adsorption of water from the gas phase on the surface of platinum was studied. The tube A, Fig. 1, is cut from the apparatus and a platinum tube, constructed to given internal dimensions, is sealed in its place. The volume is accurately determined before the tube is mounted in the apparatus. The inner surface of the platinum was polished, and thoroughly cleaned with concentrated nitric acid. The cleaning was completed by repeated washing with distilled water. The pointer F cannot be used in this experiment as the zero position at constant volume.

By the following method constant volume and constant adsorption surface of platinum were maintained. One terminal of an accumulator is connected to a voltmeter which is in turn in electrical connexion with the platinum tube, the other terminal of the accumulator is in electrical connexion with the mercury in the reservoir attached to D. When the mercury is lowered in D, the voltmeter does not register, but as soon as the mercury is raised until it touches the bottom end of the platinum tube the electrical circuit is completed and the voltmeter registers. By careful adjustment it is possible by this means to maintain a constant volume within the system.

The method of admitting water vapour to the system is identical with that already described. During each increase of temperature in a series of measurements, the mercury in F is raised a short distance into the platinum tube so that the water vapour does not adsorb on the glass surface of the tube F. When equilibrium has been established at the higher temperature, the mercury is carefully adjusted to the zero position and the pressure read as before. The methods of measuring the amounts of water adsorbed from the gas phase, and the calculations from the pressures measured, are in every case similar to those already described and need not be set out in detail here. The equation giving the free energy change is that already employed. The dimensions of the platinum tube are different from those of the glass tube, the volume being 5·317 c.c. and the area of the internal surface 15·36 sq. cm. The introduction of these values into the other equations alters the value of the constants as given below.

The measurements of pressure and the values of $N/\text{cm.}^2$, θ, and $-\Delta F$ at the corresponding temperatures are given in columns 2, 3, 4, and 5 respectively in Table II.

$$N/\text{cm.}^2 = (p/T - p_1/T_1) \times 3{\cdot}359 \times 10^{18}. \quad \theta = (p/T - p_1/T_1) \times 2824.$$

The adsorbed film of water on a platinum surface the equilibrium pressure of which is equal to the vapour pressure of water is produced

TABLE II.

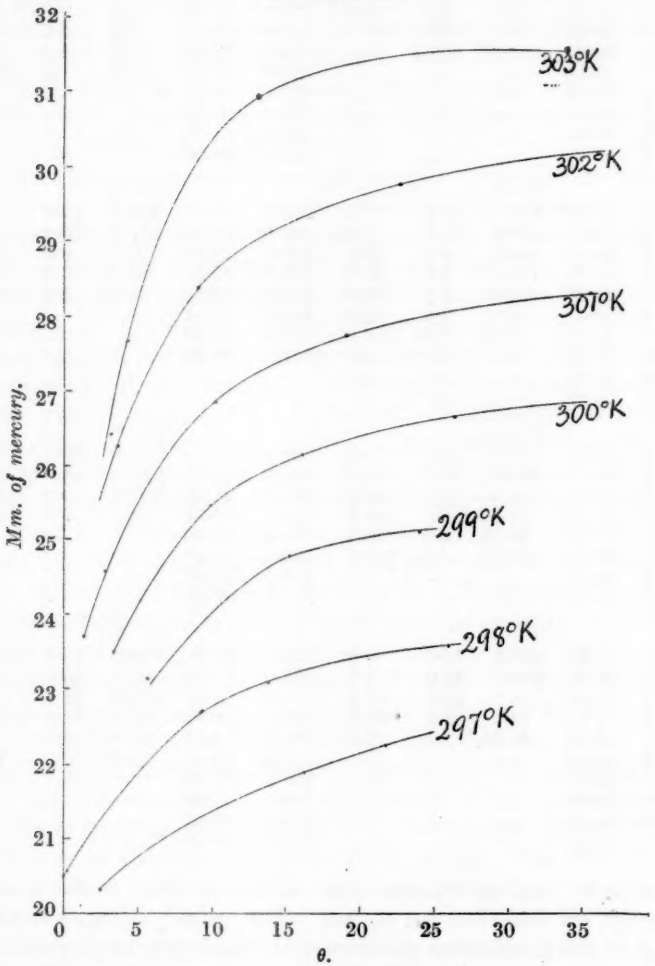
$T°$ abs.	p mm.	N/cm.^{2} $\times 10^{-14}$.	θ.	$-\Delta F$.	$T°$ abs.	p mm.	N/cm.^{2} $\times 10^{-14}$.	θ.	$-\Delta F$.
		No. 1.					No. 2.		
293·5	18·01	265·3	22·3	0·0	296·0	21·07	278·8	23·4	0·0
294·0	18·46	218·3	18·4	6·06	296·5	21·40	248·5	20·9	8·0
295·0	19·10	151·2	12·7	22·0	297·0	21·88	194·8	16·3	13·0
296·0	19·83	77·3	6·5	35·5	298·0	22·71	110·8	9·3	26·7
297·0	20·32	30·2	2·5	57·0	299·0	23·17	67·2	5·6	50·5
298·0	20·61	3·36	0·28	84·1	300·0	23·50	40·3	3·3	77·1
299·0	20·73	—	—	—	301·0	23·71	16·8	1·4	107·1
301·0	20·88	—	—	—	303·0	24·10	—	—	—
303·0	21·12	—	—	—	306·0	24·44	—	—	—
306·0	21·42	—	—	—	309·0	24·76	—	—	—
309·0	21·68	—	—	—	312·0	25·09	—	—	—
		No. 3.					No. 4.		
296·5	21·70	315·7	26·5	0·0	298·0	23·76	309·0	26·0	0·0
297·0	22·24	258·6	21·7	3·53	299·0	24·79	181·4	15·2	8·6
298·0	23·10	164·6	13·8	16·6	300·0	25·46	117·5	9·9	29·5
299·0	23·70	114·2	9·6	36·9	302·0	26·29	43·66	3·6	80·3
300·0	24·20	67·2	5·6	59·6	303·0	26·43	36·94	3·1	112·0
301·0	24·57	33·6	2·8	85·6	306·0	27·04	—	—	—
303·0	24·95	10·07	0·84	146·8	309·0	27·43	—	—	—
306·0	25·30	—	—	—	312·0	27·93	—	—	—
309·0	25·79	—	—	—					
312·0	26·10	—	—	—					
		No. 5.					No. 6.		
299·0	25·21	285·5	24·0	0·0	300·0	26·74	325·8	26·4	0·0
300·0	26·13	191·5	16·1	13·8	301·0	27·75	225·1	18·9	12·8
301·0	26·84	120·9	10·2	32·8	302·0	28·89	107·5	9·0	23·5
302·0	27·26	97·4	8·1	58·5	303·0	29·74	23·5	1·9	40·7
303·0	27·66	50·38	4·2	84·7	304·0	30·10	—	—	—
306·0	28·20	23·51	1·9	177·6	306·0	30·27	—	—	—
309·0	28·68	—	—	—	309·0	30·80	—	—	—
312·0	28·99	—	—	—	312·0	31·29	—	—	—
		No. 7.					No. 8.		
301·0	28·30	423·2	35·6	0·0	302·5	30·91	463·5	38·9	0·0
302·0	29·77	272·1	22·9	5·5	303·0	31·50	399·7	33·6	5·4
303·0	30·92	154·5	13·0	17·3	304·0	32·93	258·6	21·7	13·9
304·0	31·79	70·5	5·9	35·2	305·0	34·10	141·1	11·8	27·2
305·0	32·21	36·94	3·1	75·9	306·0	34·92	63·83	5·3	47·2
306·0	32·66	—	—	—	307·0	35·31	33·59	2·8	74·8
308·0	32·87	—	—	—	309·0	35·86	—	—	—
311·0	33·41	—	—	—	312·0	36·38	—	—	—
314·0	33·76	—	—	—	315·0	36·88	—	—	—
317·0	34·03	—	—	—	318·0	37·43	—	—	—

according to varying temperatures when from 265·3 to 325·8 $\times$ 10^{14} molecules are adsorbed per sq. cm. The curves in Fig. 4 show the change in the equilibrium pressure of the film with varying thickness at constant temperature. The limiting pressure value of adsorption measurements at any one temperature is the normal vapour pressure of water at that temperature. Hence the highest pressure on each isotherm is the vapour pressure of water at that temperature. It is evident from the shape of these isothermal curves that they will all cut the ordinate axis at a finite pressure. It follows that below

these pressures measurable adsorption of the type studied here does not occur. These pressures where the adsorption first begins cannot be measured directly, but the extrapolation of these curves

FIG. 4.

Platinum–water.



would give this pressure. The value so obtained from the 298°-isotherm is 20·50 mm. The isotherms above 298° abs. will cut the pressure axis above this point. The extrapolation of the other curves is unwarranted. It is possible that a stable film of adsorbed water is present on the platinum surface whose equilibrium pressure

is too small to be measured by this means. If this is actually the case, the true value of the molecular thickness would be $\theta + n$, where n is the number of molecular layers in the stable film. However, allowing for the possible existence of a stable film on the surface, we may still say that adsorption of the type studied here begins at a finite pressure.

The adsorption on glass is much greater than on platinum. The free energy change accompanying adsorption on a glass surface is much greater than that on a platinum surface.

The results given here are in good agreement with those of other investigators working at similar pressures and temperatures and with similar surfaces but by different methods.

The best of these are probably those of Ihmori (*loc. cit.*), who studied the adsorption of water on a plane Jena glass surface. He states the thickness of the adsorbed film on a glass surface to be from 0·3 to $4{\cdot}0 \times 10^{-6}$ cm. Our results show the film to be from 0·0 to $5{\cdot}3 \times 10^{-6}$ cm. thick. His value for platinum is from 0·0 to $1{\cdot}2 \times 10^{-6}$ cm., whilst ours is 0·0 to $1{\cdot}13 \times 10^{-6}$ cm. Other investigators, working with powdered substances or with glass wool, have obtained consistently higher values than these. These large adsorption values are due to the difficulties involved in calculating the surface of a finely-powdered substance and to capillary and sorption effects. As the adsorption measured here is a reversible equilibrium, it cannot be due to solid solution or chemical combination.

This work is being extended by one of us to other surfaces and vapours.

Summary.

(1) A new method has been devised for measuring the adsorption of vapours on solid surfaces.

(2) The adsorption of water vapour on a glass and a platinum surface has been studied.

(3) The number of molecules adsorbed per sq. cm. has been accurately determined and this value for an adsorbed film, the equilibrium pressure of which is equal to that of the vapour pressure of water, has been determined for glass and platinum surfaces.

(4) The change in free energy accompanying adsorption of water from the gaseous phase on glass and platinum surfaces at various temperatures and different numbers of molecules per sq. cm. adsorbed has been calculated.

(5) The magnitudes of the adsorption of water from the gaseous phase on glass and on platinum surfaces have been compared qualitatively.

(6) Experimental results show, in the case of water vapour on a platinum surface, that this type of adsorption begins at a finite pressure.

The authors wish to express to Prof. F. G. Donnan their appreciation of the interest he has taken in this research.

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CCIX.—*A New Method of Diagnosing Potential Optical Activity. Part I. The Optical Activity of Chlorobromomethanesulphonic Acid.*

By JOHN READ and ANN MORTIMER MCMATH.

THE difficulty of obtaining satisfactory experimental evidence of the actual or potential existence of optically active forms, corresponding with enantiomorphous modifications, of substances possessing fewer than three carbon atoms in the molecule is well known. Despite repeated attempts on the part of numerous investigators, the accounts of which have doubtlessly remained to a large extent unpublished, it was not until forty years after the promulgation of Le Bel and van 't Hoff's theory of the spatial molecular configuration of carbon compounds that incontrovertible proof was forthcoming of the capacity of substances of such simple molecular constitution to exist in optically active enantiomorphous modifications. Even yet, chloroiodomethanesulphonic acid, $CHClI{\cdot}SO_3H$, resolved into optically active components by Pope and Read in 1914 (J., **105**, 811), provides the sole example of the existence of a one carbon-atom molecule in optically active modifications. Since failure to resolve such simple asymmetrically constituted substances had been hitherto ascribed to their ready racemisation, the extraordinarily pronounced optical stability of the active forms of chloroiodomethanesulphonic acid (*loc. cit.*, p. 819) provided a striking and unexpected contrast to Swarts' description of the presumed immediate racemisation of fluorochlorobromoacetic acid when liberated from combination with strychnine (*Bull. Acad. roy. Belg.*, 1896, **31**, 28; "Mémoires couronnés," 1896, 54), and Porcher's account of the fleeting activity of chlorosulphoacetic acid (*Bull. Soc. chim.*, 1903, **27**, 438).

Many seeming anomalies remained after the optical resolution of chloroiodomethanesulphonic acid, one of the most striking being

the lack of success to resolve chlorobromomethanesulphonic acid (compare Pope and Read, J., 1908, **93**, 797). This substance bears the closest conceivable constitutional relationship to chloroiodomethanesulphonic acid, and also, as described below, forms a brucine salt distinguished by an almost identical sparing solubility. Nevertheless, repeated attempts to prepare optically active specimens of the bromo-acid or its salts by fractional precipitation with brucine, according to the method applied successfully to the iodo-acid, resulted in failure. In seeking a reason for this apparent anomaly, it appeared very improbable, in the light of the observations recorded for the iodo-acid, that any explanation could be based upon extreme facility of racemisation; but before exploring other lines of inquiry it was felt advisable to submit this possibility to more stringent tests than have been as yet applied in investigations of the kind. In further experiments with brucine and strychnine, the possible racemising action of heat and alkaline reagents was avoided as far as possible by producing the alkaloidal salts from aqueous solutions at the ordinary temperature and decomposing the various fractions with the minimum amount of cold dilute ammonia; no resolution, however, could be established in this way.*

In view of the possible catalytic racemising action of water upon a presumed highly mobile asymmetric system, attempts were next made to carry out the processes as completely as possible in organic solvents. The very sparing solubility of the brucine salt appeared unfavourable for such a purpose, and eventually hydroxyhydrindamine was selected as a base likely to yield a salt capable of ready fractional crystallisation from a suitable series of organic solvents (Pope and Read, J., 1912, **101**, 760). Preliminary experiments showed that no resolution could be accomplished by using this base in aqueous solution. The salt prepared by mixing equivalent amounts of the free acid and *l*-hydroxyhydrindamine in presence of acetone containing traces of water crystallised without difficulty, and exhibited two widely distinct kinds of crystals at the first recrystallisation from this solvent: a preliminary separation of compact, glistening plates was succeeded in the supernatant mother-liquor by a radiating mass of long, silky needles; and upon carrying out a lengthy fractional crystallisation these two forms recurred,

* These experiments, carried out at intervals over a long period but hitherto unpublished owing to the inconclusive results, were completed prior to the publication of the recent paper by Backer and Burgers (this vol., p. 233) describing the successful adoption of very similar precautions in the apparently partial optical resolution of chlorosulphoacetic acid. The chlorobromomethanesulphonic acid used in the preliminary work was kindly made available several years ago by Sir William Pope.

any particular fraction consisting as a rule of one type only. The plates, when carefully recrystallised from acetone, separated in magnificent and highly lustrous crystals of tabular habit; whilst the needles maintained their characteristics when recrystallised from glacial acetic acid: the description below indicates their widely different morphological characteristics. Further examination disclosed the remarkable fact that the needles when recrystallised from acetone of ordinary purity separated mainly in the tabular form, whilst the plates when recrystallised from glacial acetic acid yielded nothing but needles; moreover, both kinds of crystals decomposed at practically the same temperature (187°), although the tabular form exhibited a preliminary change in appearance well below this point (160°). The relationship would therefore be ascribed in the ordinary way to the occurrence of dimorphism; and, indeed, the general appearance of the two kinds of crystals in the original separation was strongly reminiscent of the dimorphic forms of *p*-bromoacetanilide, as pictured by Chattaway and Lambert (J., 1915, **107**, 1766). Upon fuller examination, however, the plates and needles, although both giving a molecular rotatory power in dilute aqueous solution equivalent to that of the basic ion, were found to display widely different rotatory powers in organic solvents. Further, the plates, which gave the higher numerical values, exhibited marked downward mutarotation * in these solvents, the final value being in each case practically identical with the value observed for the needles in the same solvent. No mutarotation was evident in aqueous solution. Of all the organic solvents available, the plates gave the highest numerical values in pure dry acetone; moreover, the needles, which otherwise displayed little tendency towards mutarotation, showed a rapid upward change in this solvent until the attainment of the final value given by the plates in the same solvent. In all instances, the crystalline residues obtained by ordinary evaporation of the above solutions on the water-bath gave the rotatory powers characteristic of the needles, when redissolved in the various solvents indicated.

After further investigations, described below, these results were interpreted by assuming that the plates and needles represent salts of *l*-hydroxyhydrindamine with *l*- and *dl*-chlorobromomethanesulphonic acid, respectively. The main measurements of molecular rotatory power may now be summarised in the following

* For the sake of brevity the term "mutarotation" is used throughout this paper to denote the observed progressive changes in rotatory power, although possibly it would be preferable to use a distinctive word for changes of the special nature here concerned.

table, in which the above salts are designated by the respective symbols *lBlA* and *lBdlA* :

Solvent.	Salt *lBlA*. Original $M[\alpha]_D$.	Salt *lBlA*. Final $M[\alpha]_D$.	Salt *lBdlA*. Original $M[\alpha]_D$.	Salt *lBdlA*. Final $M[\alpha]_D$.	Calculated $M[\alpha]_D$ for *lA*.	Calculated $M[\alpha]_D$ for *lBdA*.
Methyl alcohol (absolute)	−180°	−71°	−71°	−71°	−109°	+38°
Ethyl alcohol (99·5%)	−180	−90	−75	−83	−105	+30
Acetone (pure anhydrous) ...	−256	−187	−71	−187	−185	+114
Glacial acetic acid	−184	−66	−59	−59	−125	+ 66
Water	−60	−60	−60	−60	—	—

The values in water are practically coincident with the value ±60·5° recorded for the basic ion in dilute aqueous solution (J., 1912, **101**, 770).

It has been observed that the active hydroxyhydrindamines, more particularly in combination with weak acids, exhibit mutarotation in certain organic solvents (*loc. cit.*, p. 759); but the slight changes recorded below for *l*-hydroxyhydrindamine benzenesulphonate and *d*-hydroxyhydrindamine acetate disclose no similarity to the very sharply defined changes now under discussion. Further, the quantitative relationships explained below and the fact that marked differences persist in new salts prepared from the two *l*-hydroxyhydrindamine salts by displacement of the base do not permit of the mutarotation being referred to tautomeric change on the part either of the base or the acid.

In order to account for the experimental observations described in this paper we revert to the original view that asymmetric carbon compounds of simple molecular constitution are as a rule exceedingly susceptible to racemisation, owing to the mobility of the groups attached to the asymmetric atom. Moreover, we now advance the new idea, as applied to such compounds, that facile racemisation involves the complementary possibility of equally facile optical stabilisation, or " deracemisation," under appropriate conditions. Thus, a very labile asymmetric molecule, when submitted to a suitable asymmetric influence, will be transformed more or less completely into one of the two possible active modifications; but when the asymmetric influence is removed, the form present in excess will undergo auto-racemisation. In the example under notice, the most effective asymmetric influence yet discovered is provided by optically active hydroxyhydrindamine in acetone solution : the *l*-base transforms the *dl*-acid largely to *l*-acid, whilst the *d*-base transforms it in the same proportion to *d*-acid. An equilibrium is thus set up in the solution between

the diastereoisomeric salts *lBlA* and *lBdA* (or *dBdA* and *dBlA*), greatly to the advantage of the former. Upon dissolving the pure solid salt, *lBlA* (or *dBdA*), in various other organic solvents, a more or less rapid racemisation of the active acid occurs, resulting as a rule in the complete, or almost complete, conversion of the salt *lBlA* (or *dBdA*) into the partially racemic salt *lBdlA* (or *dBdlA*); moreover, it has been shown that the racemisation is accelerated remarkably by the addition of small quantities of water to the solvent. Thus, in 99·5% ethyl alcohol the downward mutarotation extended over a period of 23 hours, whereas in 90% ethyl alcohol it was complete in 12 minutes.

All the recorded observations were made at the ordinary temperature, and the only solvents submitted to special purification were methyl alcohol and acetone for use in making standard determinations of optical rotatory power. For purposes of recrystallisation, acetone of the purity necessary for ordinary analytical operations was used. More detailed observations, involving the use of carefully purified solvents at a constant temperature and a study of the effect of water and other catalysts, will be carried out in due course.

The results recorded for solutions in 99·5% ethyl alcohol and glacial acetic acid suggest that even in these solvents a state of equilibrium is attained between the salts *lBlA* and *lBdA*, which does not correspond with the presence of equimolecular proportions of the two salts. Thus, in 99·5% ethyl alcohol, the value of $M[\alpha]_D$ for the pure salt *lBlA* declined from $-180°$ to $-90°$, whilst the value for *lBdlA* rose from $-75°$ to $-83°$. Accepting $-90°$ as the equilibrium value, and $-180°$ as the value for the pure salt *lBlA*, this observation corresponds with an optical equilibrium mixture composed of 57% of *lBlA* and 43% of *lBdA*, or 14% of *lBlA* and 86% of *lBdlA*. The values observed in pure dry acetone solution leave no doubt as to the existence in this solvent of an equilibrium between the two diastereoisomeric salts, *lBlA* and *lBdA*, the former predominating considerably in amount. Equilibrium is attained in this solvent with great rapidity from either side. The salt *lBlA* showed a downward mutarotation from the original value $M[\alpha]_D = -256°$ until the attainment of the equilibrium value, $M[\alpha]_D = -187°$, in about an hour; on the other hand, the partially racemic salt, *lBdlA*, exhibited an upward mutarotation from the original value, $M[\alpha]_D = -71°$, to the same equilibrium value. The upward change appeared to take slightly longer than the downward one, but more refined measurements will be needed to establish this point definitely. The curves in Fig. 2 illustrate the main trend of these and other changes.

It is thus clear that in acetone solutions of the concentrations examined, the diastereoisomeric salts, *lBlA* and *lBdA* (or *dBdA* and *dBlA*), exist in dynamic equilibrium at the ordinary temperature in the proportion of about 81% of the former to 19% of the latter, and that by careful crystallisation the whole of the original *dl*-acid may be obtained in the form *lBlA* (or *dBdA*). In effect, although not strictly in accordance with definition, this result is tantamount to a partial asymmetric synthesis with complete theoretical efficiency. The following schemes represent (i) the usual course of events in the optical resolution of an externally compensated acid by a lævorotatory base, and (ii) the optical resolution of *dl*-chlorobromomethanesulphonic acid by *l*-hydroxyhydrindamine in acetone solution, under the conditions indicated :

$$\text{(i)}\quad 2lB + dAlA = \underset{50\%}{lBlA} + \underset{50\%}{lBdA}.$$

$$\text{(ii)}\quad 2lB + dAlA = \underset{81\%}{lBlA} \rightleftharpoons \underset{19\%}{lBdA}.$$

No displacement in the equilibrium was observed on diluting the solution in pure acetone from about 0·6 to 0·15%.

The progress of the separation of crystals of *l*-hydroxyhydrindamine *l*-chlorobromomethanesulphonate from a solution in ordinary acetone of *l*-hydroxyhydrindamine *dl*-chlorobromomethanesulphonate was traced by a periodical examination, during the crystallisation, of the salt remaining in the mother-liquor : the results showed that, in accordance with anticipation, the mother-liquor contained a large excess of the salt *lBlA* throughout the process. The lowest value observed for the residual dissolved salt was − 122°, corresponding with a mixture of 64% of *lBlA* with 36% of *lBdA*, notwithstanding the presence of traces of water in the acetone.

Owing to the insolubility of the salts in benzene, chloroform, etc., no observations have yet been practicable in non-miscible solvents. Neither of the salts exhibited any change in optical rotatory power when heated at 110° for 2 hours, but the salt *lBlA* showed a marked decline, indicative of partial racemisation, when kept at 160° for ½ hour. The tabular crystals of this salt lose their transparency when kept, but as yet no accompanying change in the rotatory power of the dissolved substance has been noticed.

By subtracting the molecular rotatory power of the salt *lBdlA* from that of the salt *lBlA*, determined in the same solvent under precisely similar conditions, a value is obtained for the molecular rotation exerted by the acid part of the molecule of the second salt; the values recorded in the fifth column of the above table were calculated in this way. The values given in the last column

for the salt *lBdA* have also been deduced algebraically from the values observed for the same two salts, listed respectively in the first and third columns. It is not desired to emphasise unduly the numerical significance of the values thus derived, nor to compare them in point of precision with ionic values; yet, in view of their common method of derivation, they afford an indication of the relative order of magnitude of corresponding molecular rotatory powers in different solvents. Moreover, results of great interest have been obtained by comparing the values for chlorobromomethanesulphonic acid with values derived in a similar way for chloroiodomethanesulphonic acid. For this purpose, determinations of the molecular rotatory powers, hitherto unavailable, of *d*- and *l*-hydroxyhydrindamine *d*-chloroiodomethanesulphonate were made in absolute methyl alcohol, glacial acetic acid, and acetone, in solutions having a concentration of about 1%. These two salts were prepared for the purpose from a specimen of barium *d*-chloroiodomethanesulphonate having $M[\alpha]_D = +37{\cdot}7°$ in 1% aqueous solution, and neither of the salts was purified by fractional crystallisation. No mutarotation was observed in any instance. The observed and derived values immediately concerned are tabulated below:

	$M[\alpha]_D$ of hydroxyhydrindamine salt of				$M[\alpha]_D$ derived for	
	Bromo-acid.		Iodo-acid.		Bromo-	Iodo-
Solvent.	*lBlA*.	*lBdlA*.	*dBdA*.	*lBdA*.	acid.	acid.
Methyl alcohol (absolute)	−180°	−71°	+122°	−35°	−109°	+44°
Glacial acetic acid	−184	−59	+118	−27	−125	+46
Acetone (pure) .	−256	−71	+192	−42	−185	+75

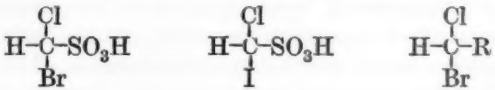
Thus, for both acids, the salts *dAdB* (or *lAlB*) yield the highest molecular rotatory power in acetone, whilst the values in methyl alcohol and acetic acid are considerably lower and practically identical in each instance for the two solvents. The ratio between the derived values of $M[\alpha]_D$ given in the last two columns is 2·5/1 in methyl alcohol, 2·7/1 in acetic acid, and 2·5/1 in acetone. Adopting a mean ratio 2·6/1, the calculated molecular rotatory power of the ion of chlorobromomethanesulphonic acid in dilute aqueous solution would thus be $M[\alpha]_D = \pm 98°$, based on the corresponding value observed for the ion of the iodo-acid, namely, $M[\alpha]_D = 37{\cdot}7°$, noted above.

Although chloroiodomethanesulphonic acid may not yet have been obtained optically pure, it is evident that a remarkable enhancement of molecular rotatory power attends the substitution of bromine for iodine in this simple molecule, and it will be a matter

of considerable interest to trace the quantitative optical effect of similar substitutions by means of a further application of the method now indicated.

The relationship just elucidated between the molecular rotatory powers of the hydroxyhydrindamine salts of these two acids appears even more striking when it is added that prior to making the above determinations of rotatory power for the salts of the iodo-acid we had failed to notice any downward mutarotation of *l*-hydroxyhydrindamine *l*-chlorobromomethanesulphonate when dissolved in acetone of ordinary purity. The constant value $M[\alpha]_D = -158°$, originally observed, was thus assumed to represent the molecular rotatory power of the pure salt *lBlA* in acetone. This value, taken in conjunction with the original value observed in the same solvent for the salt *lBdlA* (— 93°), led to the derived value $M[\alpha]_D = -64°$ for *lA*, whereas the above ratio 2·6/1 indicated $M[\alpha]_D = -194°$. It seemed likely, therefore, that the value for the pure salt *lBlA* was very much higher than $M[\alpha]_D = -158°$, and that the latter value had been attained through a rapid downward mutarotation to a point of equilibrium prior to polarimetric examination. By using scrupulously purified acetone and making the first polarimetric observation within 3 minutes of the first contact of solid with solvent, we were eventually successful in obtaining an initial value of $M[\alpha]_D = -256°$ for this salt, and in detecting the anticipated rapid fall to the equilibrium value; moreover, the initial value for the pure salt *lBdlA* was reduced in a similar way from — 93° to — 71°. The value of $M[\alpha]_D$ for *lA* thereby became — 186°, in place of the value — 64° first deduced, and thus approximated very closely to the anticipated value, — 194°.

The optical effect of configuration (I) thus appears to be numerically about 2·6 times as great as that of (II), and the high values observed in the present investigation also exhibit a notable contrast to the feeble optical activity recorded for 4-chloro-1-methyl*cyclo*hexyl-4-chlorobromoacetic acid and 4-chloro-1-methyl-4-chlorobromomethyl*cyclo*hexane ($M[\alpha]_D = 3°$ and 0·9°, respectively, in ethyl alcohol; see Perkin and Pope, J., 1911, **99**, 1527), which may be derived theoretically from configuration (I) by replacing the simple group SO_3H by a large complex radical, R (III) :



(I.) (II.) (III.)

It is suggested that the low molecular rotatory powers exhibited by configurations (II) and (III) may be due largely to a steric

effect: comparing (I) and (II), the substitution of I for Br would leave less of the environment of the carbon atom available for H, Cl, and SO_3H; whilst, comparing (I) and (III), the substitution of R for SO_3H would lead to a still more pronounced curtailment of the space available for H, Cl, and Br. It will be interesting to investigate this idea further by the examination of other asymmetric substances of analogous constitution.

When separated from the optically active base, chlorobromomethanesulphonic acid racemises with extreme ease. Although the asymmetric influence of the base enables a distinctive crystalline β-naphthylamine salt to be isolated from *l*-hydroxyhydrindamine *l*-chlorobromomethanesulphonate, in admixture with β-naphthylamine dissolved in glacial acetic acid, the salt shows no optical activity immediately after solution in organic solvents, and when recovered from the solvent has undergone transformation into the β-naphthylamine salt deposited directly from a mixture of β-naphthylamine and *l*-hydroxyhydrindamine *dl*-chlorobromomethanesulphonate in glacial acetic acid.

Extremely interesting results were obtained by precipitating the various hydroxyhydrindamine salts by the addition of brucine acetate in acetone solution. The salt *lBlA* yielded a dextrorotatory brucine salt which gave a maximum original value of $[\alpha]_D = +6{\cdot}8°$ in glacial acetic acid solution, changing rapidly to a maximum lævorotation of $[\alpha]_D = -10{\cdot}4°$. The corresponding values for the brucine salt precipitated from the salt *lBdlA* were $-8{\cdot}0°$ and $-11{\cdot}2°$, respectively. The dextrorotation of the brucine salt *lBlA* was also established in acetone solution. Since it transpired that salts of brucine with inactive acids of closely related constitution evinced no measurable optical activity when dissolved in glacial acetic acid under similar conditions, the optical effects noticed in the above determinations must be ascribed to the chlorobromomethanesulphonic acid. Two important points then emerge. In the first place, the brucine salts, like the hydroxyhydrindamine salts, exhibit mutarotation, in this instance rising in a lævo-sense in glacial acetic acid; so that, unlike *l*-hydroxyhydrindamine, brucine appears to stabilise a pronounced excess of the lævo-modification of the acid in glacial acetic acid solution. Secondly, the exchange of bases appears to be accompanied by optical inversion on the part of the acid. In the latter event, it was anticipated that *d*-hydroxyhydrindamine *d*-chlorobromomethanesulphonate, although containing the dextrorotatory acid, would fail to yield a dextrorotatory brucine salt. A further experiment confirmed this supposition, the first value observed for this brucine salt being $[\alpha]_D = -6{\cdot}6°$, rising in 90 minutes to a maxi-

mum value of $-10{\cdot}0°$. These curious phenomena of optical inversion, reminiscent in some ways of the Walden change, will be submitted to further investigation; but, in general, polarimetric observations on the brucine salts are rendered difficult owing to their very sparing solubility, and consequent small optical rotation, even in glacial acetic acid. The application of heat is necessary to effect solution, and in all instances this process occasions mutarotation towards zero, since the active brucine salts lose their rotatory power completely when heated on the water-bath in glacial acetic acid solution for 2 or 3 hours. In the course of the investigation of the brucine salts of chlorobromomethanesulphonic acid, evidence was obtained indicating that the salt of the inactive acid is the least soluble of the various salts or mixtures of salts possible: it would therefore be impracticable in any case to resolve the acid by fractional precipitation with this base.

By using *d*-hydroxyhydrindamine the salts *dBdA* and *dBdlA* were readily prepared in a similar manner, and these were proved experimentally to be respectively enantiomorphous with the above-mentioned salts *lBlA* and *lBdlA*. By mixing equal weights of *dBdA* and *lBdlA* in absolute methyl alcohol, and thus annulling the optical rotation due to the basic portions of the molecules, it was possible to demonstrate a slowly fading optical activity on the part of the acid present. The first value observed, $M[\alpha]_D = +49°$, agrees well with the calculated value, $+108°/2$. Chlorobromomethanesulphonic acid is thus the simplest substance which has yet been proved capable of exhibiting optical activity in the amorphous condition. The activity vanished completely in 32 hours, the racemisation being much more rapid than in the case of the salt *dBdA* (or *lBlA*), in which a powerful restraint appears to be exerted on the process by the full equivalent of *d*- (or *l*-) base present.

According to the views which have now found mention, the production of two wholly racemic salts might be anticipated, one of which would separate on mixing either salt of the *d*-base with either salt of the *l*-base in acetone, and the other of which would be deposited by crystallising a similar mixture from glacial acetic acid. These expectations were realised, the first racemate, *lBlA* . *dBdA*, crystallising in glassy prisms, and the second, *lBlA*,*lBdA* . *dBdA*,*dBlA*, in short, glistening needles. Morphologically, the racemates resemble the component salts very closely, but are more soluble and have lower melting points.

Close parallels to the results now brought forward are to be discerned in the work of McKenzie and Smith (J., 1923, **123**, 1962; 1924, **125**, 1582) on catalytic racemisation. These authors have

shown, for example, that *l*-menthyl *d*-phenylchloroacetate, through the catalytic action of a drop of alcoholic alkali, passes into an equilibrium mixture containing a preponderating amount of *l*-menthyl *l*-phenylchloroacetate. They have also established (*Ber.*, 1925, **58**, 894) the directing influence of an optically active terpene group in converting a mixture of equal amounts of diastereoisomeric menthyl (or bornyl) esters quantitatively into a mixture of unequal amounts of the same esters; thus, the addition of a trace of alcoholic alkali to a mixture of equal quantities of *l*-menthyl *d*-phenylchloroacetate and *l*-menthyl *l*-phenylchloroacetate causes the latter ester to preponderate (57%) without any analytical separation having been effected. Similarly, in the present investigation it appears that water exerts a powerful catalytic action which in most solvents results in the final production of equal, or very nearly equal, amounts of the two diastereoisomeric salts, *lBlA* and *lBdA* (or *dBdA* and *dBlA*); in acetone solution, however, the equilibrium is displaced strongly in favour of the first salt, and the actual position of the equilibrium would appear to be influenced *inter alia* by the amount of water present. It seems likely that in all instances the asymmetric directing influence of the optically active hydroxyhydrindamine becomes operative through the interposition of a catalytic agent, which may well prove to be water, even in the carefully dried acetone used in making the more refined observations recorded herewith.

An example of the general principle we now outline for simple asymmetric carbon compounds is provided in the case of the asymmetric tin atom by the well-known investigations of Pope and Peachey on methylethylpropylstannonium *d*-camphorsulphonate and *d*-bromocamphorsulphonate: evaporation of aqueous solutions of these salts led in each instance to the deposition of the single substance, *dBdA*, owing to progressive racemisation of the salt remaining in the mother-liquor (P., 1900, **16**, 42, 116; compare also Mills and Bain, J., 1910, **97**, 1866). In the case of the active salts *lBlA* and *dBdA* now under consideration, a partly racemic salt of the type *l*(or *d*)*BdlA* was usually left upon evaporating solutions in acetone containing a little water, although under certain conditions an excess of the original salt was found in the residue. The deposited salts of the tin compound were, however, characterised by sparing solubility, whereas with the hydroxyhydrindamine chlorobromomethanesulphonates no deposition occurs from warm acetone containing small amounts of water until most of the solvent has volatilised. No evidence has been adduced of the stabilisation of an excess of one form of the optically active stannonium compound in solution, the mother-liquor of the salt

dBdA being apparently a solution of the partial racemate *dlBdA*; the solvent concerned in this instance, however, is water, which instantly racemises *d*- or *l*-chlorobromomethanesulphonic acid, even when combined with optically active hydroxyhydrindamine.

The conception of extreme mobility of the simple atoms or groups attached to an isolated carbon atom also accords with Le Bel's hypothesis of a similar mobility of groups in asymmetric quinquevalent nitrogen compounds of simple molecular constitution, and with the observations of A. Werner and others on the ready racemisation of asymmetric assemblages associated with isolated atoms of cobalt, chromium, etc. Further, it affords an explanation of the difficulties experienced in preparing optically active substances containing fewer than three carbon atoms in the molecule, and is in agreement with the fugitive optical activity in aqueous solution of chlorosulphoacetic acid and its salts, indicated by Porcher (*loc. cit.*) and recently demonstrated by Backer and Burgers (this vol., p. 233). Incidentally, the suggestion that the variations in rotatory power shown by different fractions of the normal *d*-hydroxyhydrindamine salt of this acid indicated its partial resolution is also upheld (Pope and Read, J., 1914, **105**, 814). We anticipate that asymmetric compounds containing two carbon atoms in the molecule will also display phenomena of the kind now described, and thus lend themselves to preparation for the first time in optically pure combinations by treatment with optically active bases in organic solvents. Through a systematic application of the method to asymmetric compounds of simple molecular constitution, it is hoped to gather much new information respecting the comparative mobility of groups in systems of the kind.

It seems worthy of note that in the case of the optically active tin derivatives prepared by Pope and Peachey, the two dextrorotatory acids employed each imposed a dextrorotatory orientation upon the asymmetric complex involved. Similarly, in the present investigation, dextrorotatory hydroxyhydrindamine gives rise to dextrorotatory chlorobromomethanesulphonic acid, whilst lævorotatory hydroxyhydrindamine and lævorotatory brucine each favour a lævorotatory configuration of the associated asymmetric system. It will be interesting to ascertain whether any generalisation is possible on this basis, especially in view of the fact, to which attention may be directed, that in the closely related process of partial asymmetric synthesis the optically active product exhibits in the great majority of instances the same sense of rotation as the directive asymmetric system. Thus, *l*-brucine hydrogen methylethylmalonate yields an excess of the *l*-valerate when heated

(Marckwald, *Ber.*, 1904, **37**, 349); *l*-menthyl benzoylformate upon reduction gives an excess of the *l*-mandelate, and upon treatment with magnesium methyl iodide an excess of *l*-phenylmethylglycollate; whilst from *l*-menthyl pyruvate a lævorotatory lactic acid may be prepared by reduction; moreover, the *l*-bornyl group sometimes exerts a less pronounced asymmetric influence than the more highly lævorotatory *l*-menthyl group (McKenzie, J., 1904, **85**, 1249; 1905, **87**, 1373; 1906, **89**, 365 and 688). The results now described afford a very definite indication of the profound influence which may be exerted by an optically active nucleus upon an associated potentially active system, and provide a close parallel to the quantitative partial asymmetric syntheses which appear to occur in nature. Moreover, in our opinion, substances possessing the readily controlled asymmetric mobility evinced by chlorobromomethanesulphonic acid are much more likely to be amenable to processes of complete asymmetric synthesis, accomplished in the absence of optically active material, than any asymmetric substances yet investigated with this object in view. We propose to submit this new idea to practical tests at a later stage in these investigations.

The enormous difference in optical stability between chlorobromomethanesulphonic acid and chloroiodomethanesulphonic acid could not have been predicted, and is difficult to explain. In both instances the great resistance offered to alkaline hydrolysis is worthy of remark. The distinction may possibly be determined to some degree by the greater atomic volume, lower mobility, and less active chemical nature of iodine as compared with bromine. Possibly also the different affinity value, evidenced by the formation of such derivatives as $Ph{\cdot}ICl_2$, has a bearing upon the matter. It is hoped to gather further evidence by an examination of the remaining dihalogenomethanesulphonic acids and various closely related substances.

In continuing this series of investigations, we reserve the application of the method described not only to compounds of the simple molecular constitution indicated above, but also to other types of organic derivatives which may be conceived to possess potential optical activity associated with high mobility of the asymmetric system and therefore unrecognisable by any of the methods hitherto utilised. The exceedingly delicate diagnostic method we now describe may well lead to the discovery of optical activity on the part of organic types which, like chlorobromomethanesulphonic acid, have as yet resisted all attempts at optical resolution.

EXPERIMENTAL.

Preparation of dl-*Chlorobromomethanesulphonic Acid.*—The crude barium salt was prepared in the manner described by Andreasch (*Monatsh.*, 1887, **7**, 159), by heating barium chlorosulphoacetate to 120—130° in a sealed tube for several hours with bromine (1 mol.) and a little water. Chloromethanesulphonic acid and other impurities were eliminated by taking advantage of the sparing solubility of brucine chlorobromomethanesulphonate. To a warm aqueous solution of the recrystallised barium salt was added a similar solution containing one-third the calculated quantity of brucine acetate or brucine hydrochloride. For an amount of salt corresponding to 30 g. of the acid a total volume of about 500 c.c. was found suitable. After keeping for several hours the crystalline separation of brucine salt was collected and washed well with cold water, whilst the filtrate was treated in a similar way with a like amount of brucine. Both separations consisted of pure brucine chlorobromomethanesulphonate; practically two-thirds of the original acid was obtained in this form, the remaining one-third being rejected. The *brucine* salt forms minute, glistening needles, which decompose at 275°. It is practically insoluble in all the ordinary solvents, the most favourable being boiling glacial acetic acid (Found: C, 47·6; H, 4·3. $C_{24}H_{28}O_7N_2ClBrS$ requires C, 47·7; H, 4·6%).

For purposes of further work the brucine salt was mixed with cold water and shaken with an excess of dilute ammonia, the brucine being extracted with chloroform; evaporation of the aqueous liquid furnished the pure ammonium salt. No optical activity could be established with specimens of the salt prepared in this way. The *ammonium* salt is freely soluble in water or alcohol and sparingly soluble in warm acetone. It is best crystallised from hot glacial acetic acid, in which it is moderately soluble; it forms glistening plates, m. p. 205° (decomp.) (Found: NH_3, 7·6, 7·7. $CH_5O_3NClBrS$ requires NH_3, 7·5%). When the salt was heated under reflux for 2 hours with an excess of 10% aqueous sodium hydroxide solution, hydrolysis occurred to a slight extent only, the proportion of halogen removed being less than 2% of the total amount present.

Treatment of dl-*Chlorobromomethanesulphonic Acid with* l-*Hydroxyhydrindamine in Acetone Solution.*—An aqueous solution containing 14·7 g. of pure *dl*-chlorobromomethanesulphonic acid was evaporated as completely as possible on the water-bath in an open dish. Upon covering the partly crystalline mass with acetone (15 c.c.) and stirring in solid *l*-hydroxyhydrindamine (10·4 g.; 1 mol.), a

thick homogeneous liquid was produced, and when the stirring was continued for a short time on the water-bath the whole mass suddenly crystallised. The slightly brown, crystalline mass weighed 25·1 g. when dry. It was very soluble in water, ethyl alcohol, or methyl alcohol, moderately soluble in boiling acetone, sparingly soluble in ethyl acetate, and practically insoluble in ether, benzene, chloroform, light petroleum, etc.

A solution of the dry product in boiling acetone of ordinary purity (about 275 c.c.) and a small quantity of methyl alcohol was filtered and allowed to crystallise. The crystalline separation which accrued overnight (11 g.) consisted mainly of large, well-defined, glistening plates, but the upper part of the mother-liquor was filled with long, radiating needles. The latter dissolved readily when the fraction was separated and warmed with acetone; the undissolved residue (5·4 g.) was composed entirely of plates, which when freshly dissolved in cold methyl alcohol to form a 2·5% solution gave $[\alpha]_D = -48{\cdot}2°$, whence $M[\alpha]_D = -173°$, calculated for hydroxyhydrindamine chlorobromomethanesulphonate. The combined mother-liquors were concentrated, and the ensuing crystalline separation was subjected to a prolonged systematic fractional crystallisation from hot acetone, to which a little methyl alcohol was added when necessary. As a result, two distinct kinds of fractions were obtained, one consisting of plates and the other of needles. The plates predominated in the earlier fractions, although occasionally these yielded needles. Mother-liquors which had been repeatedly concentrated yielded needles more frequently than plates, especially when it was found necessary to accelerate the deposition of crystals by the addition of ether. The bulk of the material from the fractionation was obtained in the form of plates, although of seventeen fractions eight consisted wholly of plates and seven wholly of needles. The two kinds of crystals showed little distinction in melting point, but possessed characteristic optical rotatory powers when dissolved in organic solvents. Ordinary methyl alcohol was used as solvent in all the preliminary determinations, and the following typical result may be quoted for the plates: 0·2573 g., dissolved in methyl alcohol and made up to 20·0 c.c. at the ordinary temperature, gave $\alpha_D = -1{\cdot}24°$ when examined at once in a 2-dcm. tube, whence $[\alpha]_D = -48{\cdot}2°$, and $M[\alpha]_D = -173°$, calculated for hydroxyhydrindamine chlorobromomethanesulphonate. Other determinations of $M[\alpha]_D$ recorded for similar fractions were $-176°$, $-172°$, $-173°$, and $-172°$. In the case of a typical fraction composed of needles, 0·2550 g. when dissolved and examined under similar conditions gave $\alpha_D = -0{\cdot}51°$, whence $[\alpha]_D = -20{\cdot}0°$, and $M[\alpha]_D = -72°$.

Of the results yielded by other fractions of the same kind, the following may be quoted as representative: $M[\alpha]_D = -72°$, $-73°$, $-72°$, and $-73°$. Of the seventeen fractions examined, only two gave intermediate values, namely, $M[\alpha]_D = -119°$ and $-92°$, respectively: both these fractions were obtained by evaporating the solvent to dryness on the water-bath and inoculating the warm liquid mass with a crystal of the higher rotatory power. The final mother-liquor was dark in colour, and upon evaporation yielded a dark and somewhat tarry residue. By conversion to brucine salt and subsequent careful treatment with cold dilute ammonia, a somewhat brown specimen (1 g.) of ammonium chlorobromomethanesulphonate was prepared from the final residue; this was optically inactive in 3·5% aqueous solution when examined polarimetrically in a 2-dcm. tube in sodium light.

For the reasons stated above, the plates and needles were regarded as the *l*-hydroxyhydrindamine salts of *l*-chlorobromomethanesulphonic acid and *dl*-chlorobromomethanesulphonic acid, respectively.

l-*Hydroxyhydrindamine* l-*Chlorobromomethanesulphonate*, $C_9H_{11}ON{\cdot}CHClBr{\cdot}SO_3H$.—The various fractions of this salt obtained in the course of the fractional crystallisation were mixed and recrystallised from warm acetone containing a small quantity of methyl alcohol. No difference was apparent in the properties of the substance after this treatment. Under the proper conditions the salt crystallises with remarkable facility and may be readily obtained in lustrous, tabular crystals, measuring up to 1 cm. in length. Through the courtesy of Mr. T. V. Barker, the following crystallographic description and goniometric characterisation of the substance have been kindly furnished by Miss Marie Bentivoglio, of the Department of Mineralogy, University of Oxford, to whom we express our grateful thanks:

"*l*-Hydroxyhydrindamine *l*-chlorobromomethanesulphonate forms colourless crystals which become opaque when kept for a few weeks. The habit is tabular, parallel to *a* (100); sometimes two *q* (011) faces are large and two prisms suppressed, so that the crystal appears polar.

"The crystals belong to the monoclinic system, and the elements are $a : b : c = 1{\cdot}3246 : 1 : 1{\cdot}0780$; $\beta = 114° 19'$.

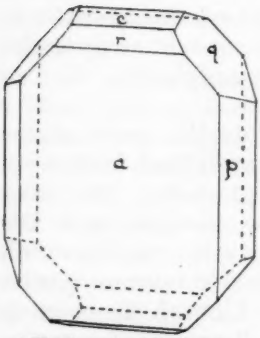
"The forms present are *a*, *p*, *c*, *r*, *q* (Fig. 1), and these have the following values:

	a (100).	*p* (110).	*c* (001).	*q* (011).	*r* (101).
ϕ.....	90° 0′	*39° 38′	90° 0′	23° 07′	90° 0′
.....	90 0	90 0	*24 19	*49 27	57 20 (16)

"Refractive index = 1·50."

l-Hydroxyhydrindamine *l*-chlorobromomethanesulphonate dissolves freely in water, or in methyl or ethyl alcohol at the ordinary temperature; it also dissolves readily in glacial acetic acid, and is moderately soluble in boiling acetone. It is very slightly soluble in hot ethyl acetate, but is practically undissolved by chloroform, benzene, ether, or light petroleum. It can only be recrystallised with certainty from warm acetone, to which the addition of a little methyl alcohol is permissible; as the solvent cools, the salt separates rapidly in the characteristic form, the initial deposition being facilitated in the case of a sterile solution by inoculation. When the acetone mother-liquors are allowed to evaporate to dryness in an open space at the ordinary temperature, the final separation usually consists mainly of needles of the partly racemic salt. In order to ascertain the relative stability of the two salts in contact with a saturated solution in ordinary purified acetone, a mother-liquor containing both plates and needles was kept in a desiccator, and after 3 days the needles had completely disappeared, whilst the plates had grown and maintained their lustre. *l*-Hydroxyhydrindamine *l*-chlorobromomethanesulphonate has a tendency to form supersaturated solutions, from which crystallisation takes place easily upon inoculation. Strong saturated solutions in warm methyl alcohol of ordinary purity redeposit the salt of the *l*-acid if cooled rapidly, but otherwise nothing but the partially racemic salt can be obtained from such solutions. In warm glacial acetic acid the salt of the *l*-acid is more readily soluble than the partially racemic salt, and a rapid and apparently complete conversion of the first-named salt to the second occurs in this solvent. When heated in a capillary tube, powdered *l*-hydroxyhydrindamine *l*-chlorobromomethanesulphonate loses its opacity at about 160° and decomposes at about 183° (Found: C, 33·8; H, 3·5. $C_{10}H_{13}O_4NClBrS$ requires C, 33·5; H, 3·6%).

FIG. 1.



l-Hydroxyhydrindamine l-chlorobromomethanesulphonate.

The optical rotatory powers of freshly made solutions of *l*-hydroxyhydrindamine *l*-chlorobromomethanesulphonate in the solvents utilised in the course of this investigation are summarised in the following table. The solutions were prepared as quickly as practicable, and heating was avoided if possible. With glacial acetic acid, and also with acetone at the higher concentration noted, it was found necessary, however, to warm the solvent on the water-

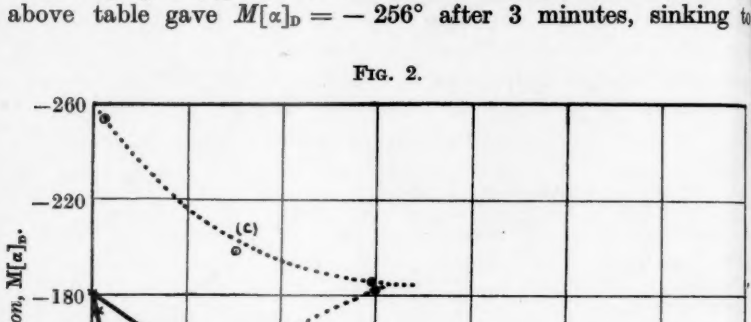
bath in order to effect solution. The interval which elapsed between the first contact with the solvent and the initial polarimetric observation was therefore appreciably longer in these two instances than in the others. The absolute methyl alcohol was dehydrated by means of metallic magnesium in presence of a trace of iodine (compare *Ber.*, 1923, **56**, 894). The "absolute" ethyl alcohol used contained about 0·5% of water. The acetone used for the original determination was of the purity required for ordinary analytical operations; but for the more dilute solutions very pure acetone was employed, which had been liberated from the sodium bisulphite compound and carefully dried and redistilled. The last-named solutions were prepared as rapidly as possible by shaking the finely powdered salt with the solvent at the ordinary temperature.

Solvent.	Approximate weight (g.) of salt in 20·0 c.c.	Time (minutes).	$[\alpha]_D$.	$M[\alpha]_D$.
Methyl alcohol (ordinary)	0·25	5	−48·6°	−174°
Methyl alcohol (absolute)	0·25	5	−50·0	−180
Ethyl alcohol (99·5%)	0·25	5	−50·0	−180
Acetone (ordinary)	0·25 (warmed)	30	−43·9	−158
Acetone (pure anhydrous)	0·10	20	−52·0	−187
Acetone (pure anhydrous)	0·05	10	−60·1	−216
Acetone (pure anhydrous)	0·025	3	−71·4	−256
Glacial acetic acid	0·25 (warmed)	10	−51·2	−184
Water	0·25	5	−16·9	− 60

All the solutions except those in water and acetone of ordinary analytical purity, which maintained their initial rotatory powers, exhibited marked downward mutarotation when kept at the ordinary temperature. The following typical series of values, selected from a mass of similar data, are sufficient to indicate the course of the changes. In methyl alcohol of ordinary purity, the initial molecular rotatory power of − 174° declined to − 115° in 14 hours, to − 97° in 24 hours, and reached a constant value of − 71° in 60 hours [Fig. 2 (*b*)]. In absolute methyl alcohol, the original value of − 180° fell to − 126° in 48 hours, − 102° in 70 hours, − 95° in 94 hours, − 86° in 146 hours, − 83° in 170 hours, and reached a constant value of − 71° in 220 hours [Fig. 2 (*a*)]. In absolute ethyl alcohol, the original value of − 180° declined to − 96° in 15 hours, and attained a final value of − 90° in 23 hours. In glacial acetic acid, the original value of − 184° fell to − 96° in 17 hours, and reached a constant value of − 66° in 35 hours.

Of these solvents, by far the slowest change thus occurred in absolute methyl alcohol. No mutarotation was apparent in a solution prepared by dissolving about 0·25 g. of the salt in warm acetone of ordinary purity, a constant value of $M[\alpha]_D = -158°$ being obtained. More dilute solutions prepared rapidly at the ordinary temperature in pure anhydrous acetone exhibited a strikingly rapid downward mutarotation to a constant value of $M[\alpha]_D = -187°$ [Fig. 2 (*c*)]. The most dilute solution indicated in the above table gave $M[\alpha]_D = -256°$ after 3 minutes, sinking to

FIG. 2.



Mutarotation of 1-*hydroxyhydrindamine chlorobromomethanesulphonates:* (a) lBlA *in absolute methyl alcohol,* (b) lBlA *in ordinary methyl alcohol,* (c) lBlA *in pure acetone,* (d) lBdlA *in pure acetone.*

$-198°$ in 35 minutes, and reaching the equilibrium value, $-187°$, in somewhat less than an hour; whilst the solution of twice this concentration gave $M[\alpha]_D = -216°$ 10 minutes after the first contact with the solvent, and $-188°$ after 45 minutes.

Upon removing the volatile solvents on the water-bath at any stage during the change, without attempting to exclude traces of water, the residue was found to consist wholly of the partly racemic salt, with a molecular rotatory power of about $-72°$ in ordinary methyl alcohol. In one instance, a residue obtained in this way from methyl alcohol was induced to crystallise on the water-bath by inoculation with a trace of the tabular form of crystal: the

molecular rotatory power of the residue thereby rose to $-87°$. The striking difference in the velocity of mutarotation exhibited by solutions in ordinary and carefully dried methyl alcohol led to an investigation of the effect upon the process of adding small quantities of water to ethyl alcohol used as a solvent in similar determinations. Such additions proved to exert a very remarkable accelerating influence upon the change. In a typical determination, 0·2500 g. of the salt when dissolved in cold 90% ethyl alcohol gave $\alpha_D = -0·79°$ 4 minutes after the first contact with the solvent, whence $[\alpha]_D = -31·6°$ and $M[\alpha]_D = -113°$. Owing to the very rapid fall in rotatory power, a second reading could not be taken conveniently until a further period of 4 minutes had elapsed, when the value observed was $\alpha_D = -0·45°$. A constant reading, $\alpha_D = -0·43°$, was reached 12 minutes after the first contact: the final value of $[\alpha]_D$ was thus $-17·2°$, and of $M[\alpha]_D$ $-62°$. A specimen of the pure powdered salt, after keeping at 160° for 30 minutes, gave $M[\alpha]_D = -149°$ when freshly dissolved in absolute methyl alcohol.

l-*Hydroxyhydrindamine* dl-*Chlorobromomethanesulphonate*.—The various fractions of the needle-shaped crystals deposited during the original series of recrystallisations were purified by a further recrystallisation from hot glacial acetic acid. Upon cooling, the solvent deposited rosettes of hard, glittering needles, which were collected and washed with ethyl acetate; further preparations of the substance were made by dissolving the tabular crystals in the same solvent, when the separation formed on cooling consisted entirely of the partially racemic salt. The crystals, which are unsuitable for goniometric examination, show straight extinction with strong double refraction. The refractive index is greater than 1·60.

The salt is much more soluble in acetone and in methyl and ethyl alcohol than the salt of the *l*-acid, and is also slightly soluble in boiling chloroform. It is practically insoluble in benzene, ether, or light petroleum. In glacial acetic acid it dissolves with greater difficulty than the isomeric salt; crystallisation occurs with great ease from this solvent, and the substance shows no tendency to form supersaturated solutions. It dissolves sparingly in boiling ethyl acetate, and separates in fine needles upon cooling. When a solution of the salt in a little hot glacial acetic acid is diluted with hot ethyl acetate the liquid gradually becomes filled with magnificent interlacing aggregates, composed of long, silky needles radiating from centres: this procedure affords the best method of purifying the substance. Moderately strong solutions of the partially racemic salt in acetone readily deposit the characteristic tabular crystals

of *l*-hydroxyhydrindamine *l*-chlorobromomethanesulphonate when allowed to cool. *l*-Hydroxyhydrindamine *dl*-chlorobromomethanesulphonate decomposes at 187° without the preliminary change noticed in the case of the other salt (Found: C, 33·7; H, 3·7. $C_{10}H_{13}O_4NClBrS$ requires C, 33·5; H, 3·6%).

Optical rotatory powers were determined in various solvents, under the conditions outlined for the isomeric salt, the concentration being approximately 0·25 g. of salt in 20·0 c.c. of solution; the resulting values agreed very closely with the corresponding values furnished by the salt of the *l*-acid after the completion of the mutarotative changes. The partially racemic salt exhibited no mutarotation in methyl alcohol, glacial acetic acid, or water. A slight upward mutarotation occurred in 99·5% ethyl alcohol, until the final value given by the isomeric salt was practically attained: the initial value, $M[\alpha]_D = -75°$, rose in 4 hours to − 80°, and in 20 hours to − 83°, and no further change was observed.

Very striking changes were traced in acetone solutions. In a preliminary series of observations, about 0·25 g. of the salt was dissolved in acetone of ordinary purity, by warming for 10 minutes on the water-bath and then making up the cooled solution to 20·0 c.c. with the solvent: the original molecular rotatory power of − 93° rose in 20 hours to − 147°, and in 27 hours to a constant value of − 154°. When evaporated to dryness on the water-bath, the solution yielded a crystalline residue which exhibited a molecular rotatory power of − 104° when freshly redissolved in acetone; after 20 hours the value had again risen to − 154°, at which it remained constant. In a similar experiment, the residue recovered by evaporation on the water-bath gave an original value of − 148° when freshly dissolved in methyl alcohol; after 40 hours, the molecular rotatory power had declined to a constant value of − 74°. When dissolved in 90% ethyl alcohol, this salt gave a constant molecular rotatory power of − 63°.

A much more rapid upward mutarotation occurred in pure anhydrous acetone: 0·1014 g. of the salt, dissolved to 20·0 c.c., gave $[\alpha]_D = -18°$, 3 minutes after the first contact with the cold solvent, whence $M[\alpha]_D = -71°$. The successive values observed after 8 minutes and 20 minutes, respectively, were $M[\alpha]_D = -89°$, and − 124°; the constant value, − 187°, attained in about an hour, is identical with the equilibrium value furnished by the isomeric salt under similar conditions [Fig. 2 (d)]. The main relationships between the molecular rotatory powers displayed by the two isomeric salts in various solvents are summarised in the following table:

Solvent.	*l*-Hydroxyhydrindamine *l*-chlorobromomethanesulphonate. Original $M[\alpha]_D$.	*l*-Hydroxyhydrindamine *l*-chlorobromomethanesulphonate. Final $M[\alpha]_D$.	*l*-Hydroxyhydrindamine *dl*-chlorobromomethanesulphonate. Original $M[\alpha]_D$.	*l*-Hydroxyhydrindamine *dl*-chlorobromomethanesulphonate. Final $M[\alpha]_D$.
Methyl alcohol (ordinary)	−174°	−71°	−72°	−72°
Methyl alcohol (absolute)	−180	−71	−71	−71
Ethyl alcohol (99·5%)	−180	−90	−75	−83
Ethyl alcohol ... (90%)	−113	−62	−63	−63
Acetone (ordinary)	−158	−158	−93	−154
Acetone (pure anhydrous) ...	−256	−187	−71	−187
Glacial acetic acid	−184	−66	−59	−59
Water	−60	−60	−60	−60

For the reasons already stated, a further examination was made into the nature of the process whereby the salt of the *dl*-acid after solution in acetone yields a separation of the isomeric salt of the *l*-acid. The partially racemic salt (4·4 g.) was dissolved in warm acetone of ordinary purity with the addition of a few drops of methyl alcohol, and upon allowing the solution to cool, a separation consisting wholly of tabular crystals was deposited. After the lapse of 50 minutes 5 c.c. of the clear mother-liquor were withdrawn, diluted to 20·0 c.c. with acetone, and examined polarimetrically in a 2-dcm. tube. By subsequently evaporating a measured portion of the diluted solution it was ascertained that the observed reading, $\alpha_D = -1{\cdot}02°$, corresponded to 0·2748 g. of the salt dissolved in 20·0 c.c. of acetone, whence $M[\alpha]_D = -131°$. After a further interval of 200 minutes, during which nothing but tabular crystals separated, 5 c.c. of the mother-liquor were found to contain 0·1790 g. of dissolved salt having a molecular rotatory power of −122°. It appears, therefore, that the solution in acetone always contains an excess of the salt *lBlA*, notwithstanding its continuous withdrawal during the process of crystallisation.

For purposes of comparison in two kinds of solvents giving rise to mutarotation, a specimen of l-*hydroxyhydrindamine benzenesulphonate* was prepared by mixing equivalent amounts of the free acid and base on the water-bath in presence of acetone containing a little water. The resulting crystalline solid separated from hot acetone containing a little methyl alcohol in clusters of glittering, anhydrous prisms, m. p. 198°, when the solution was allowed to cool (Found: C, 58·7; H, 5·7. $C_{15}H_{17}O_4NS$ requires C, 58·6; H, 5·5%).

The original molecular rotatory power of this substance in acetone

was — 140°, and a slight decline to a constant value of — 131° occurred in 20 hours. The salt recovered by evaporation on the water-bath gave a constant molecular rotatory power of — 75° in methyl alcohol. The original salt gave an initial value of — 100° in the same solvent, declining to a constant value of — 76° in 8 hours. A slight downward mutarotation was thus displayed in both types of solvent. *d*-Hydroxyhydrindamine acetate (J., 1912, **101**, 777) gave the constant value $M[\alpha]_D = +61°$ in methyl alcohol, and in acetone declined from + 414° to + 382° in 44 hours.

Replacement of the Base in l-*Hydroxyhydrindamine* l- *and* dl-*Chlorobromomethanesulphonate.*—1. When *l*-hydroxyhydrindamine *l*-chlorobromomethanesulphonate was dissolved in warm acetone containing a trace of methyl alcohol and mixed with a solution of the calculated amount of brucine acetate in warm acetone, there was an immediate separation of well-defined crystalline needles. These were collected and washed with acetone, cold water, and again with acetone; the dry product represented an almost theoretical yield of brucine chlorobromomethanesulphonate. Owing to the sparing solubility of the salt, the determination of its optical rotatory power presented considerable difficulty; but readings were eventually obtained in acetone, which dissolves it slightly, and glacial acetic acid, which is the best solvent available for the purpose. A small quantity of the salt was heated on the water-bath for 20 minutes with acetone, so that a portion remained undissolved; after keeping for 24 hours at the ordinary temperature, the clear saturated solution gave $\alpha_D = +0{\cdot}11°$ when examined polarimetrically in a 4-dcm. tube. In a further experiment, 0·1025 g. was completely dissolved in glacial acetic acid by heating on the water-bath for 25 minutes. The cold solution, when made up to 20·0 c.c. and examined forthwith in a 2-dcm. tube, gave $\alpha_D = +0{\cdot}07°$, whence $[\alpha]_D = +6{\cdot}8°$. A similar determination made upon a solution containing 0·2010 g. of the salt in 30·0 c.c. yielded the value $\alpha_D = +0{\cdot}16°$ in a 4-dcm. tube. In a third determination an identical value was observed 15 minutes after the first contact with the solvent, but in 3 hours the solution exhibited no appreciable optical activity, and further readings were rendered impossible through the separation of crystals in the polarimeter tube. In a fourth determination, made upon a new preparation of the brucine salt, the initial value, $[\alpha]_D = +6{\cdot}1°$, declined to zero in 45 minutes, to — 7·5° in 1·5 hours, and reached a constant value of — 10·4° in 3·5 hours; in this instance no crystallisation occurred. A fifth solution of the same kind when heated on the water-bath for 3 hours showed no appreciable optical activity in a 4-dcm. tube.

l-Hydroxyhydrindamine *dl*-chlorobromomethanesulphonate also yielded a brucine salt when treated in the manner described above; the two brucine salts were very similar in appearance, except that the second one crystallised in smaller needles than the first. A saturated solution of the second salt in acetone, prepared at the same time and in exactly the same manner as the corresponding solution of the first brucine salt, gave the value $\alpha_D = -0{\cdot}02°$ when examined polarimetrically in a 4-dcm. tube. This value, although difficult to establish with precision, is obviously different from the corresponding value, $\alpha_D = +0{\cdot}11°$, recorded above for the related salt. A solution of 0·1118 g. in glacial acetic acid, prepared in the manner described above and examined forthwith, gave $\alpha_D = -0{\cdot}13°$ in a 2-dcm. tube, whence $[\alpha]_D = -11{\cdot}2°$. In a second similar determination, 0·2010 g. made up to 30·0 c.c. with glacial acetic acid gave $\alpha_D = -0{\cdot}28°$ in a 4-dcm. tube, whence $[\alpha]_D = -10{\cdot}4°$. A third determination, made upon a new preparation of the brucine salt, gave an original value of $[\alpha]_D = -8{\cdot}0°$, which changed in the course of 9 hours to a constant value of $-10{\cdot}5°$. A fourth similar solution displayed no measurable optical activity after heating for 3 hours on the water-bath.

In several instances the brucine salt derived from *l*-hydroxyhydrindamine *l*-chlorobromomethanesulphonate crystallised from glacial acetic acid in the polarimeter tube, but no such behaviour was observed on the part of the second brucine salt, which thus appears to be the more soluble, or, at least, to have passed through the stage of the mutarotation corresponding to the least solubility.

Brucine *dl*-chlorobromomethanesulphonate, prepared by mixing aqueous solutions of equimolecular amounts of ammonium *dl*-chlorobromomethanesulphonate and brucine hydrochloride, dissolved with greater difficulty in hot glacial acetic acid than either of the brucine salts described above. When prepared by heating over a small flame and then examined immediately after cooling, a 0·5% solution showed no measurable optical rotation in a 2-dcm. tube, and the crystallisation of the substance in the tube rendered further observation impracticable. The various preparations of brucine salt obtained by fractional precipitation from aqueous solution showed similar behaviour when dissolved in glacial acetic acid, and thus consisted probably of brucine *dl*-chlorobromomethanesulphonate, as indicated below.

The optical inversion noticed upon precipitating *l*-hydroxyhydrindamine *l*-chlorobromomethanesulphonate with brucine acetate led to an examination of the optical rotatory power of the brucine salt prepared from an optically impure specimen of ammonium *l*-chloroiodomethanesulphonate, having $M[\alpha]_D = -28°$ in 1%

solution in glacial acetic acid. The brucine salt obtained by completely precipitating an aqueous solution of this ammonium salt by the addition of brucine hydrochloride had $M[\alpha]_D = -50°$ when dissolved to form a 0·6% solution in glacial acetic acid. No inversion was therefore apparent, and neither of these salts showed mutarotation in glacial acetic acid.

An investigation of a number of salts of brucine with optically inactive acids showed that such salts, when dissolved in glacial acetic acid to form solutions of the approximate molecular concentration indicated above, gave no measurable rotation when examined in a 4-dcm. tube in sodium light. The salts examined comprised brucine *dl*-chloroiodomethanesulphonate, brucine sulphate, and brucine benzenesulphonate. As a check, it was noted that the specimen of brucine sulphate used was appreciably active in 1% aqueous solution, the values observed being $[\alpha]_D = -24·4°$, and $M[\alpha]_D = -121°$ (Found: SO_4, 9·63; loss at 115° in 30 hours, 11·16. $B_2,H_2SO_4,6H_2O$ requires SO_4, 9·66; H_2O, 10·88%). *Brucine benzenesulphonate*, prepared by mixing the acid and base in presence of water and evaporating to dryness, crystallises from hot methyl alcohol, in which it is moderately soluble, in rosettes of glistening, anhydrous needles.

2. Of the many attempts made to replace the *l*-hydroxyhydrindamine in the above salts by an optically inactive base, avoiding water as a solvent, success was only achieved with benzidine and β-naphthylamine. Upon dissolving either of the *l*-hydroxyhydrindamine salts, with very gentle warming, in about ten times the weight of glacial acetic acid and adding at once to the cooled solution an equivalent quantity of benzidine dissolved in a like volume of the same solvent, an immediate and practically quantitative precipitation of the corresponding benzidine salt occurred. In each instance the salt consisted of minute needles, practically insoluble in water, acetone, or glacial acetic acid, and only slightly soluble in alcohol. About 0·1 g. of each salt was dissolved separately in absolute methyl alcohol on the water-bath, the cold solution being then made up to 20·0 c.c. with the solvent. About 10 minutes elapsed between first contact of the material with the solvent and the polarimetric observation, and no optical activity was observed in either instance.

3. The β-naphthylamine salts were prepared in a similar way, except that smaller amounts of glacial acetic acid were used. The β-naphthylamine salt obtained from *l*-hydroxyhydrindamine *l*-chlorobromomethanesulphonate was a crystalline powder, consisting of minute, glistening prisms, m. p. 210—240° (decomp.). The β-naphthylamine salt prepared from *l*-hydroxyhydrindamine *dl*-chloro-

bromomethanesulphonate was quite distinct in appearance from the salt just described: it consisted of well-defined, silky needles, which decomposed very definitely at 240°, without undergoing any preliminary change. The distinctions were confirmed by carrying out a second preparation of each salt. Neither of the β-naphthylamine salts was soluble in benzene or chloroform, but both were readily soluble in cold acetone or alcohol, and moderately soluble in warm glacial acetic acid. The salt obtained from the *dl*-acid appeared to be less soluble than the other, and either salt upon recrystallisation from glacial acetic acid yielded silky needles decomposing at 240°.

In each case, 0·15 g. of the original β-naphthylamine salt, when dissolved in cold acetone and made up to 20·0 c.c. with the solvent, failed to reveal any optical activity when examined polarimetrically in a 2-dcm. tube 5 minutes after the first contact with the solvent. A similar result was obtained by dissolving 0·2 g. in absolute methyl alcohol in an exactly similar manner. The residues recovered from the acetone and methyl alcohol solutions by allowing the solvent to evaporate at the ordinary temperature were identical in appearance.

d-*Hydroxyhydrindamine* d-*Chlorobromomethanesulphonate.*—A crystalline mass was readily obtained by mixing equivalent quantities of *d*-hydroxyhydrindamine and *dl*-chlorobromomethanesulphonic acid on the water-bath in presence of a little acetone, as described above for the *l*-base. When the product was recrystallised from warm acetone containing a little methyl alcohol, it yielded glistening plates, identical in appearance with crystals of *l*-hydroxyhydrindamine *l*-chlorobromomethanesulphonate: 0·2000 g. dissolved in absolute methyl alcohol at the ordinary temperature and made up to 20·0 c.c., gave $\alpha_D = +1{\cdot}00°$, when examined at once in a 2-dcm. tube, whence $[\alpha]_D = +50{\cdot}0°$, and $M[\alpha]_D = +180°$. The two salts crystallising in tabular form are thus enantiomorphously related. When the above solution was evaporated to dryness on the water-bath, the residue gave $M[\alpha]_D = +71°$ when redissolved in absolute methyl alcohol: the analogy between the enantiomorphous salts is thus complete.

The brucine salt derived from *d*-hydroxyhydrindamine *d*-chlorobromomethanesulphonate by precipitation in acetone solution was not noticeably different in appearance or solubility from the brucine salt derived in a similar way from the enantiomorphous substance. In this instance, however, no dextrorotation could be established by dissolving the brucine salt in glacial acetic acid: 0·1510 g., when dissolved in a few minutes by heating the solvent over a small flame and examined forthwith in the usual way, gave $\alpha_D =$

$-0{\cdot}10°$ in a 2-dcm. tube, whence $[\alpha]_D = -6{\cdot}6°$. A constant value of $[\alpha]_D = -10{\cdot}0°$ was attained after an interval of 90 minutes.

d-*Hydroxyhydrindamine* dl-*Chlorobromomethanesulphonate*.—The acetone mother-liquor from the salt just described was evaporated to dryness on the water-bath and the residue recrystallised from a small quantity of hot glacial acetic acid, with the addition of hot ethyl acetate in excess: the resulting long, silky needles gave a constant value of $M[\alpha]_D = +71°$ when dissolved in absolute methyl alcohol at the usual concentration, and exhibited the expected upward mutarotation when dissolved in acetone.

Wholly Racemic Forms of Hydroxyhydrindamine Chlorobromomethanesulphonate.—A solution of a mixture of equal weights of *l*- and *d*-hydroxyhydrindamine *dl*-chlorobromomethanesulphonate in a small amount of hot glacial acetic acid was diluted with hot ethyl acetate and allowed to cool. The crystalline separation which gradually ensued consisted wholly of rosettes of short, glistening needles. The substance, which was optically inactive, softened slightly at 155°, melted without decomposition at 175°, and recrystallised on cooling. In appearance it was very similar to *l*- or *d*-hydroxyhydrindamine *dl*-chlorobromomethanesulphonate, but was more soluble than these salts. The same substance resulted when a mixture of equal weights of *d*-hydroxyhydrindamine *d*-chlorobromomethanesulphonate and *l*-hydroxyhydrindamine *l*-chlorobromomethanesulphonate was treated similarly.

Upon crystallising the last-named mixture from acetone, in place of acetic acid, the resulting crystalline deposit contained the form of racemate just described, interspersed with large, glassy, transparent prisms, very similar in appearance to the original salts. These crystals, which melted at 160° and recrystallised on cooling, represented a second completely racemic form. A similar mixed deposit of needles and large prisms was also obtained by recrystallising the first racemic form from acetone. The interconversions shown by the constituent optically active salts thus persist in the racemates.

Exhibition of Optical Activity by Chlorobromomethanesulphonic Acid in Combination with an Optically Inactive Base.—Although no optical activity could be established when *l*(or *d*)-hydroxyhydrindamine in combination with *l*(or *d*)-chlorobromomethanesulphonic acid was replaced by a new optically inactive base, it was found that the optical activity of the acid in these salts persisted for a while when the activity of the combined hydroxyhydrindamine was neutralised by the addition of an equal weight of the salt containing the opposed optical form of this base in combination with the racemic acid. As an example, a mixture of

0·2024 g. of *d*-hydroxyhydrindamine *d*-chlorobromomethanesulphonate with 0·2024 g. of *l*-hydroxyhydrindamine *dl*-chlorobromomethanesulphonate was dissolved in cold absolute methyl alcohol and made up to 20·0 c.c. with the solvent. When examined in a 2-dcm. tube, 2 minutes after the first contact, an optical rotation of $\alpha_D = +0{\cdot}55°$ was observed, whence $[\alpha]_D = +13{\cdot}6°$, and $M[\alpha]_D = +49°$. In 4·5 hours the value of $M[\alpha]_D$ had declined to + 33°, in 7·25 hours to + 31°, in 28 hours to + 8°, and in 32 hours the optical activity had completely disappeared. The rate of change was thus considerably more rapid than that exhibited in the later stages of the mutarotation of *l*-hydroxyhydrindamine *l*-chlorobromomethanesulphonate in the same solvent.

The investigation will be extended, as occasion permits, in the various directions indicated. We express our acknowledgments to the Department of Scientific and Industrial Research for a maintenance grant to one of the authors (A.M.M.).

UNITED COLLEGE, THE UNIVERSITY,
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CCX.—*The Nitration of* m-*Chlorophenol.*

By HERBERT HENRY HODGSON and FRANCIS HARRY MOORE.

THE scanty literature on this subject prior to 1924 deals only with 3-chloro-6-nitrophenol (Laubenheimer, *Ber.*, 1876, **9**, 76; Uhlemann, *Ber.*, 1878, **11**, 1161), 3-chloro-4 : 6-dinitrophenol (Fries, *Annalen*, 1912, **389**, 305), and 3-chloro-2 : 4 : 6-trinitrophenol. Auwers and Deines (*Zentr.*, 1924, II, No. 18) have prepared 6- and 4-nitro-3-chlorophenols *via* the action of nitrous acid on 3-chloroaniline nitrate, but we have obtained very moderate yields by their method.

The present paper relating to the nitro-derivatives obtainable from *m*-chlorophenol by direct nitration is part of a systematic study of the chemistry of *m*-halogenated phenols.

The above mononitro-compounds have been prepared in purer form than any hitherto described and 3-*chloro-2-nitrophenol* has been obtained in excellent yield. 4 : 6-, 2 : 6-, and 2 : 4-Dinitro-3-chlorophenols are readily distinguishable by means of their characteristic silver salts.

Monosulphonation of *m*-chlorophenol at 100—120° appears to form exclusively 3-chlorophenol-4-sulphonic acid, owing to the usual directing influence of the hydroxyl group.

3-Chloro-2 : 4 : 6-trinitrophenol is obtained in a very pure con-

dition by the direct nitration of *m*-chlorophenol and removal of any dinitro-compound in steam. If, however, *m*-chlorophenol is sulphonated and then treated with an excess of nitric acid, a trinitro-sulphonic acid is formed which on hydrolysis yields 3-chloro-2 : 5 : 6-trinitrophenol as a product volatile in steam.

Evidence in support of the constitution assigned to 3-chloro-4-nitrosophenol by Hodgson and Moore (J., 1923, **123**, 2499) has been obtained by its oxidation to 3-chloro-4-nitrophenol.

Experimental.

Mononitration of m-*Chlorophenol.*

6- *and* 4-*Nitro*-3-*chlorophenols.*—*m*-Chlorophenol (24 g.), liquefied by alcohol (2 c.c.), was added slowly to a solution, kept below 25°, of 40 g. of concentrated sulphuric acid and 29 g. of sodium nitrate in 70 c.c. of water. After being stirred for 2 hours, the mixture was diluted with water (2 vols.). The solid was washed and steam-distilled. The yellow oil in the distillate solidified and after being pressed was again distilled in steam, when 3-chloro-6-nitrophenol, m. p. 41°, was obtained (Auwers and Deines, *loc. cit.*, give 39°) (Found : Cl, 20·4. Calc., Cl, 20·5%). The yield of crude product was 22%.

3-Chloro-4-nitrophenol, which remained in the distillation flask as a brown solid, m. p. 80—106° (yield 60%), crystallised in white, feathery needles, m. p. 121—122°, from dilute hydrochloric acid or water (Found : Cl, 20·4%). Auwers and Deines (*loc. cit.*) obtained faintly yellow needles, m. p. 120—121°, from benzene; the colour was possibly due to the action of atmospheric ammonia. We cannot confirm Uhlemann's statement (*loc. cit.*) that 3-chloro-6-nitrophenol melts at a second determination at 32° and regains its normal m. p. after several days.

Oxidation of 3-*Chloro*-4-*nitrosophenol.*—A solution of the nitrosophenol (2 g.) in 400 c.c. of water containing 20 g. of sodium hydroxide and 20 g. of potassium ferricyanide was acidified with sulphuric acid after being kept for 2 days. Ether extracted from the mixture a trace of a product which was volatile in steam and gave a red sodium salt, but the bulk of the extract was 3-chloro-4-nitrophenol, which melted at 121° after crystallisation from water (Found : Cl, 20·3%).

Oxidation with nitric acid of various strengths and with hydrogen peroxide produced similar results, but the yields were unsatisfactory.

3-*Chloro*-2-*nitrophenol.*—*m*-Chlorophenol (12·8 g.) was added slowly to 75 g. of oleum (27% SO_3), cooled after each addition.

The mixture was kept for 12 hours and then heated for 2 hours on a water-bath to complete the disulphonation. Nitric acid (4·5 c.c.; *d* 1·5) dissolved in 20 c.c. of oleum (27% SO_3) was added during 15 minutes to the cooled mixture, which was then kept for 2 hours. On dilution and hydrolysis in a current of steam, a viscous, yellow, opaque oil passed over which rapidly solidified; it separated in white, slender needles, m. p. 37·5°, from its yellow solution in light petroleum (yield 11 g.; 66%) (Found: Cl, 20·35. $C_6H_4O_3NCl$ requires Cl, 20·5%).

3-Chloro-2-nitrophenol is remarkable as being an *o*-nitrophenol which is colourless. It is readily turned yellow by atmospheric ammonia. Like its 6-nitro-isomeride, it has a distinctive odour; the 4-nitro-isomeride is odourless. The *silver* salt of 3-chloro-2-nitrophenol forms characteristic crimson festoons (Found: Ag, 38·2. $C_6H_3O_3NClAg$ requires Ag, 38·5%). The *methyl* ether was prepared by means of boiling aqueous sodium carbonate and excess of methyl sulphate. The product was steam-distilled and the white solid crystallised from dilute alcohol; m. p. 55° (Found: Cl, 18·7. $C_7H_6O_3NCl$ requires Cl, 18·9%). The *benzoate* could not be prepared in aqueous alkali hydroxide, but was readily obtained in aqueous sodium carbonate. It separated from alcohol in colourless crystals, m. p. 123° (Found: Cl, 12·1. $C_{13}H_8O_4NCl$ requires Cl, 12·7%).

Dinitration of m-*Chlorophenols.*

General Procedure.—The initial material is added gradually to a cooled mixed acid containing 98% sulphuric acid (15 vols.), 70% nitric acid (12 vols.), and water (9 vols.). After an interval, the mixture is warmed if necessary, diluted, and steam-distilled. The dinitro-products are all volatile with steam and crystallise well from water or dilute acids.

3-*Chloro*-4 : 6-*dinitrophenol.*—(*a*) The reaction mixture (1 g. of 3-chloro-6-nitrophenol and 3 c.c. of mixed acid; 3 c.c. of concentrated sulphuric acid were subsequently added) was kept for 2 hours and then heated for ½ hour on the water-bath. 3-Chloro-4 : 6-dinitrophenol was obtained in colourless crystals, m. p. 92—93°, from water or in stout prisms from light petroleum (Found: Cl, 16·1. Calc., Cl, 16·2%). A non-volatile product was 3-chloro-2 : 4 : 6-trinitrophenol, large, white needles, m. p. 114° (from water).

(*b*) The reaction mixture (1 g. of 3-chloro-4-nitrophenol and 4 c.c. of mixed acid) was kept over the week-end. The product had m. p. 92—93° (Found: Cl, 16·15%).

(*c*) 1 : 3-Dichloro-4 : 6-dinitrobenzene was boiled with aqueous sodium carbonate, and the solution acidified after filtration. The precipitate melted at 92° after being crystallised from water.

The identity of the three products in (*a*), (*b*), and (*c*) was established by the melting points of their mixtures.

3-*Chloro*-2 : 6-*dinitrophenol*.—(*a*) This was obtained from a reaction mixture of 2 g. of 3-chloro-2-nitrophenol and 12 c.c. of mixed acid. It is less volatile with steam than its 4 : 6-dinitro-isomeride and crystallises from dilute hydrochloric acid in white, feathery crystals, m. p. 114·5° (Found : Cl, 16·1. Calc., Cl, 16·2%). A non-volatile product was 3-chloro-2 : 4 : 6-trinitrophenol (Found : Cl, 13·2. Calc., Cl, 13·5%).

(*b*) A mixture of 4 g. of 3-chloro-2-nitrophenol and 4 c.c. of oleum (27% SO_3) was kept over-night (crystals of unchanged material separated), 4 c.c. of oleum were added and, 4 hours later, the mixture was heated on the water-bath to complete the sulphonation. It was then nitrated with 1 c.c. of nitric acid (*d* 1·5) dissolved in 2·5 c.c. of oleum. The product volatile with steam was 3-chloro-2 : 6-dinitrophenol. The liquor in the flask, on neutralisation with potassium carbonate, gave a bright yellow potassium salt (probably of 3-chloro-2 : 6-dinitrophenol-4-sulphonic acid) from which 3-chloro-2 : 6-dinitrophenol was obtained on hydrolysis.

(*c*) A mixture of 3 g. of *m*-chlorophenol and 7 c.c. of oleum (27% SO_3), after being kept for 2 hours, was nitrated with 0·8 c.c. of nitric acid (*d* 1·5) in 4 c.c. of oleum and kept for 1 hour. The volatile product of hydrolysis by steam was 3-chloro-2 : 6-dinitrophenol (mixed m. p.).

3-*Chloro*-2 : 4-*dinitrophenol*.—After 3 g. of 3-chloro-2-nitrophenol had been added slowly to 1·8 c.c. of sulphuric acid (100%) and 4 c.c. of oleum (27% SO_3), the mixture was kept for 6 hours, then heated on the water-bath for 2 hours, cooled, nitrated with 0·8 c.c. of nitric acid (*d* 1·5) in 4 c.c. of oleum, and kept for 1 hour. The steam-distillate, on cooling, deposited 3-chloro-2 : 6-dinitrophenol. The filtrate from this, on extraction with ether, gave up a solid, probably 3-chloro-2 : 4-dinitrophenol, which, after repeated fractional crystallisation from water, had m. p. 138—140° and gave a yellow silver salt insoluble in ammonia (Found : Cl, 15·9. Calc., Cl, 16·2%).

Direct Nitration of Disulphonated m-*Chlorophenol*.—After remaining for 20 hours at 10—15°, a solution of 4·2 g. of *m*-chlorophenol in 25 g. of oleum (27% SO_3) was nitrated with 2·7 c.c. of nitric acid (*d* 1·5) in 14 c.c. of oleum and kept for 1 hour. On hydrolysis in a current of steam, 3-chloro-2-nitrophenol distilled over first and was followed by 3-chloro-2 : 6-dinitrophenol, which separated, and 3-chloro-2 : 4-dinitrophenol, which was extracted with ether, from the distillate. The presence of 3-chloro-4 : 6-dinitrophenol was not detected.

Sulphonation and Nitration of 3-*Chloro*-4-*nitrophenol*.—A solution of 5 g. of the chloronitrophenol in 10 c.c. of oleum (27% SO_3) was cooled and immediately nitrated with 1·2 c.c. of nitric acid (*d* 1·5) in 5 c.c. of oleum. After the usual treatment 3-chloro-4 : 6-dinitrophenol, but not 3-chloro-2 : 4-dinitrophenol, was obtained. If, however, the sulphonation mixture was kept for 2 hours, or was warmed, before being nitrated, no 3-chloro-4 : 6-dinitrophenol was produced, the destruction of 3-chloro-4-nitrophenol by oleum being thus made manifest. 2- and 6-Nitro-3-chlorophenol are stable towards oleum.

Properties of the Dinitro-m-*chlorophenols*.—4 : 6-, 2 : 6-, and 2 : 4-Dinitro-3-chlorophenol are in the order of increasing solubility in water. The solutions are yellow. The silver salts are prepared from the ammonium salts and silver nitrate in neutral aqueous solution. The 4 : 6-dinitro-compound gives a characteristic yellow gel which slowly becomes crystalline (Found : Ag, 33·0. Calc., Ag, 33·2%). The 2 : 4-dinitro-compound forms yellow crystals (Found : Ag, 32·95%). The 2 : 6-dinitro-compound gives a red, crystalline substance which is much more soluble in aqueous ammonia or water than either of the other two (Found : Ag, 32·9%). The silver salts of 2 : 6-dinitrophenol and 4-chloro-2 : 6-dinitrophenol also are red.

The three dinitro-*m*-chlorophenols resist methylation and benzoylation by direct means. The mononitro-compounds are methylated only with difficulty.

Trinitration of m-*Chlorophenol*.

3-*Chloro*-2 : 4 : 6-*trinitrophenol*.—*m*-Chlorophenol (4 g.) dissolved in 6 c.c. of oleum (27% SO_3) was nitrated in the cold with 40 c.c. of nitric acid (70%), added gradually. The mixture, having been stirred for 1 hour, was gently boiled for 10 minutes and poured on to ice, and products volatile with steam (if any) were removed. The residue crystallised from dilute sulphuric acid in fern-like crystals and from water in rectangular prisms, m. p. 114° (Found : Cl, 13·2. Calc., Cl, 13·5%).

3-Chloro-2 : 4 : 6-trinitrophenol is readily soluble in alcohol, ether, benzene, or chloroform. Its sodium and silver salts are yellow; the former is moderately soluble in water, and the latter insoluble in aqueous ammonia. It is the ultimate product of nitration of all the mono- and di-nitro-3-chlorophenols mentioned above.

3-*Chloro*-2 : 5 : 6-*trinitrophenol*.—*m*-Chlorophenol (5 g.) dissolved in concentrated sulphuric acid (3 c.c.) was heated for 9 hours at 120°, cooled, and poured into 50 c.c. of water. The solution was

filtered from tar, treated with 15 c.c. of nitric acid (*d* 1·5), and, after being stirred for 30 minutes, was slowly heated and finally boiled for 5 minutes. Neutralisation of the cooled filtered solution with solid potassium carbonate caused the precipitation of a yellow product, which crystallised from water in characteristic old-gold clusters and from alcohol, in which it was moderately soluble, in small, yellow needles [Found: S, 7·5; Cl, 8·0. Calc. for $C_6Cl(OK)(NO_2)_3{\cdot}SO_3K$, S, 7·6; Cl, 8·5%]. This salt was hydrolysed with boiling dilute sulphuric acid in a current of steam, and the volatile product, m. p. 112·5—113·5°, being somewhat soluble in water, was extracted from the distillate with ether (yield 2·7 g.) (Found: Cl, 13·2; N, 16·5. $C_6H_2O_7N_3Cl$ requires Cl, 13·5; N, 15·9%). The yellow, crystalline silver salt is insoluble in aqueous ammonia.

This steam-volatile trinitro-compound, produced from a monosulphonic acid in which the sulpho-group appears to be in position 4, is probably 3-chloro-2 : 5 : 6-trinitrophenol.

Traces of 4 : 6- and 2 : 4-dinitro-3-chlorophenol were detected when the original nitration mixture was steam-distilled without previous neutralisation.

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CCXI.—*Polynuclear Heterocyclic Aromatic Types. Part II. Some Anhydronium Bases.*

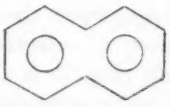
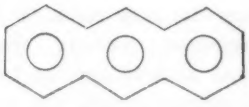
By JAMES WILSON ARMIT and ROBERT ROBINSON.

IT is a commonplace of the electronic theory of the atom and of valency that certain systems of electrons exist which by their association reach a stable condition, and an example may be found in the electron pair or duplet, the octet and dodecet, as well as in the special configurations, which are frequently assumed, of the valency electrons in nitrogen, carbon monoxide, and similar substances. The occurrence of many atoms in a molecule provides further opportunities for the emergence of electron groups of marked stability and, *ceteris paribus*, the possession of such groups confers chemical stability as shown, for example, by reduced unsaturation and a tendency to maintain the type. These are, of course, the chief characteristics of benzenoid systems, and here the explanation is obviously that six electrons are able to form a group which

resists disruption, and may be called the *aromatic sextet*.* It is not supposed that the existence of the sextet involves a change in the total covalency exerted by the carbon atoms of the ring nor does the theory as employed below require any particular assumption in regard to the position of the electrons or their orbits in space. Thus the symbols

and

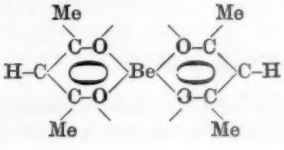
are each considered to express a view of one aspect of the problem and are not inconsistent. The first expression suggests a symmetrical distribution of electrons in the ring, and in regard to the covalencies should be taken as the interpretation of the second expression. The circle in the ring symbolises the view that six electrons in the benzene molecule produce a stable association which is responsible for the *aromatic* character of the substance.† Naphthalene and anthracene will be represented by the following formulæ

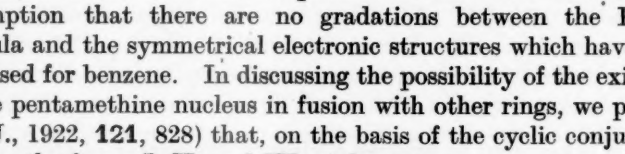
in which the deletion of the central connecting bonds is more apparent than real, because these attachments are by covalencies which involve the electrons of the sextets only. The aromatic character of thiophen and pyrrole requires the hetero-element to have contributed some of its free salt-forming electrons for the purpose of setting up a sextet, with the natural result that the basic character of these substances has been suppressed or largely diminished. In pyridine, the sextet can, however, be obtained without the help of the *lone pair* on the nitrogen atom. The

* In the ions of carboxylic acids, in the *cyclo*pentadienes and indene derivatives, and in many other types of *semi-aromatic* compounds, groups of two or four electrons may be assumed to occur.

† The stability of beryllium acetylacetone and similar substances may be associated with the fact that the rings are aromatic and contain sextets. This is possible if the function of all the oxygen atoms is assumed to be identical as in the annexed formula.

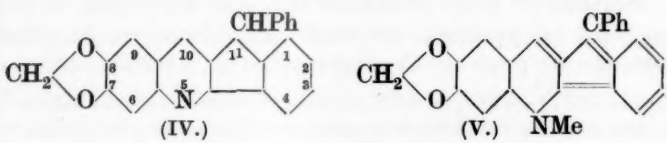


formulæ with sextets do not necessarily represent systems the aromatic character of which is of the most perfected kind. There is ample evidence that in some typical aromatic compounds the valency is unevenly distributed, and consideration of such a series as pyridine, benzene, naphthalene, anthracene, glyoxaline, thiophen, pyrrole, and furan serves to protect us from the unwarranted assumption that there are no gradations between the Kekulé formula and the symmetrical electronic structures which have been proposed for benzene. In discussing the possibility of the existence of the pentamethine nucleus in fusion with other rings, we pointed out (J., 1922, **121**, 828) that, on the basis of the cyclic conjugation theory, the forms I, II, and III might occur.



(I) (II) (III.)

On applying the restriction on the cyclic conjugation theory which is now suggested, namely, that the number of electrons must be such that sextets can be formed in each ring, it is clear that II and III cannot satisfy the condition.* The type represented by I remains theoretically possible, and we have prepared a compound which appears to contain such a nucleus. 6-Aminopiperonal and 3-phenylindanone condensed in alcoholic solution with the aid of potassium hydroxide, producing the quinoline derivative (IV), the methosulphate of which yields, on decomposition with hot aqueous alcoholic potassium hydroxide, the anhydronium base (V).

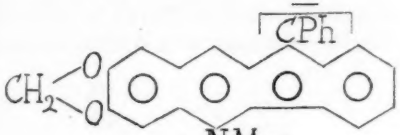


(IV.) (V.)

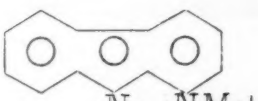
Utilising the free electrons on the nitrogen atom, 24 electrons are available for aromatic sextet formation as shown in (VI). Here the quadrivalent nitrogen is positively charged, whilst the pentamethine ring is negatively charged; (V) and (VI) represent extreme conditions, and the true structure doubtless lies between the two. (V) is not stable, because the right-hand benzene ring is

* The unsaturated nature of *cyclo*octatetraene suggests that a stable group of eight electrons analogous to the aromatic sextet is not formed.

not aromatic, and (VI) is not stable because it is a dipole; the tendencies to aromatic sextet formation and to neutralisation of the charges work in opposite directions and must reach some compromise. There is a very large class of substances which can similarly be regarded as normally occupying an intermediate position between a fully polarised aromatic phase and a neutralised quinonoid or ethenoid phase and these are usually anhydro-derivatives of aromatic *onium* hydroxides of various kinds. We propose to term these compounds *anhydronium bases*, since, although extremely diverse in form, they exhibit very similar chemical properties. Anhydronium bases derived from the methohydroxides of 4-carboline derivatives have been already described (Perkin and Robinson, J., 1919, **115**, 951; Kermack, Perkin, and Robinson, J., 1922, **121**, 1877; Robinson and Robinson, J., 1924, **125**, 832), whilst, in addition, 5-methyl-5-*iso*carboline has been recently prepared (Robinson and Thornley, J., 1924, **125**, 2169). We have now shown that 3-carboline methohydroxide loses water with the formation of an anhydride (VII). A corresponding substance in

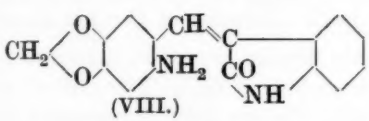


(VI)

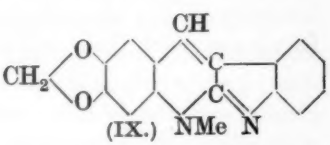


(VII)

the quinindoline series was obtained indirectly by condensation of 6-aminopiperonal with oxindole followed by treatment of the resulting aminopiperonylideneoxindole (VIII) with methyl sulphate and then with alcoholic potassium hydroxide, closing the ring with elimination of water.



(VIII.)

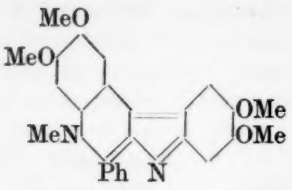


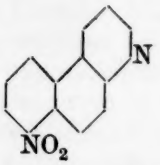
(IX.)

The base (IX) is represented in the quinonoid form, but it will be understood that we regard its actual mean condition as being something intermediate between this and the arrangement analogous to (VII). This remark applies to all formulæ here presented whether in the full polar aromatic conditions or as quinones. A bright scarlet anhydronium base in the 4-carboline series (harmine type) has been prepared by the decomposition of phenyldiveratro-

harmyrine methosulphate with sodium hydroxide and has the constitution (X).

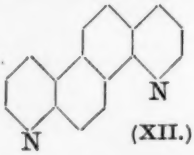
(X.)



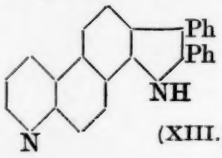


(XI.)

Anhydronium bases of what is fundamentally the glyoxaline or pyrazole type can therefore be obtained in the 3-, 4-, or 5-carboline series, the two nitrogen atoms in different rings being separated by one, two, or three carbon atoms. It was of interest to find out whether much greater separation is possible and experiments were undertaken with this object. The nitration of β-naphthaquinoline was studied by Claus and Besseler (*J. pr. Chem.*, 1898, **57**, 49), but the constitution of the mononitro-derivative was not determined. We have oriented the substance (XI) by the observation that the related aminonaphthaquinoline is converted by an application of the Skraup reaction into a naphthadiquinoline (XII), which may also be obtained from 1 : 6-naphthylenediamine in a similar manner.

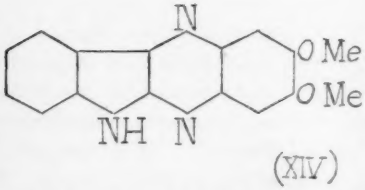


(XII.)

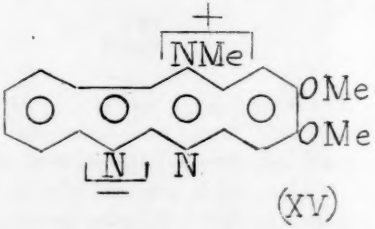


(XIII.)

Amino-β-naphthaquinoline was changed to an indole derivative (XIII) by condensation with benzoin under conditions similar to those used by Japp and Murray (**J.**, 1894, **65**, 889) in analogous cases. The results obtained on decomposing the methosulphate of (XIII) were ambiguous and indicated oxidation. We have also investigated the alkylation of an indophenazine derivative (XIV). In view of such facts as the weak basic character of the amidines



(XIV)

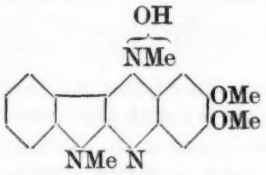


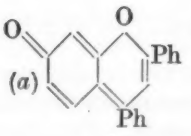
(XV)

and the circumstance that *p*-phenylenediamine is a stronger base than the *m*-isomeride, it seems most probable that the first methyl

group will attach itself to the quinoxaline nitrogen which is the more remote from the nitrogen of the indole nucleus, but there is no direct proof of this. On such an assumption, the anhydronium base derived from the methohydroxide of (XIV) will have the constitution (XV). This orange-red substance can be converted into a remarkably stable methohydroxide (XVI).

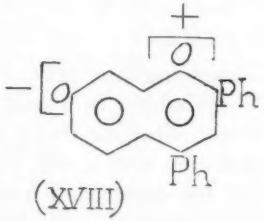
(XVI.)



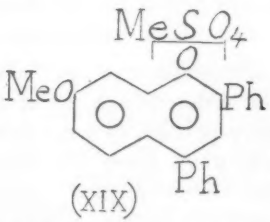


(XVII.)

It has already been stated that the anhydronium bases include many types and among these are the glyoxalines, pyrazoles, α- and γ-aminopyridines, α- and γ-pyridones, α- and γ-pyrones, carbolines and *iso*carbolines, diazo-oxides and diazoimines * derived from *o*- and *p*-hydroxy- and amino-diazonium hydroxides, fuchsones and fuchsonimines, quinopyridanes, pyranhydrones, derivatives of methylenexanthane, etc. Thus the anhydropyranol (XVII) can also be represented as a phenol-betaine (XVIII), and it is the anhydr-



(XVIII)



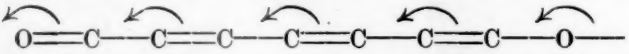
(XIX)

onium base derived from hydroxydiphenylbenzopyrylium hydroxide. As such, it shows the normal behaviour of its type and adds on methyl sulphate so as to form the pyrylium salt (XIX) by direct addition of a methyl group to the quasiquinonoid oxygen atom.

Finally, it is necessary to indicate an important consideration. The formation of an anhydronium base invariably involves a redistribution of the charge unless the positive and negative centres in the dipole are so powerfully basic and acidic that the substance is definitely a betaine. It is convenient to keep the latter separate and to reserve the expression *anhydronium base* for the compounds which are recognisably intermediate between neutral and fully polarised forms. The redistribution of charge referred to can only

* On this hypothesis, the action of methyl iodide on a diazo-oxide or diazoimine should result in the replacement of the diazo-group by iodine and the simultaneous attachment of methyl to oxygen or nitrogen, respectively.

take place if the system connecting the charged centres is a conducting system. In other words, the necessary changes in covalency must be, not merely possible, but facile, and this will be the case only with definitely conjugated systems. There must always be a possible mechanism for the transfer of the charge in accordance with the electronic theory of conjugation as in the scheme:



and this will be the case if the formula of the substance can be constructed on the classical valency theory with alternate single and double bonds. For example, if the oxygen in (XVII) is at (*a*), the condition cannot be satisfied, and therefore 6-hydroxy-2 : 4-diphenylbenzopyrylium hydroxide should not yield an anhydronium base, although it might give a betaine on the model of (XVIII). The conception of the electrical conductivity of conjugated systems is implicit in all the suggestions relating to the mechanism of addition to such systems made by Kermack and Robinson (J., 1922, **121**, 427), and for experimental evidence we can turn to graphite, each one of the layers of which must be regarded as comprising a single fully conjugated aromatic system.

EXPERIMENTAL.

7 : 8 - *Methylenedioxy* - 11 - *phenylindenoquinoline* (IV).—Aqueous potassium hydroxide (5 c.c of 50%) was added to a cold solution of 6-aminopiperonal (3·9 g.) and 3-phenylindanone (5·1 g.) in ethyl alcohol (45 c.c.), when the liquid darkened and a red, crystalline precipitate slowly formed. Next day the separation had become copious and the substance was collected, washed with alcohol, and dried at 100° (6·6 g.). The compound crystallises from benzene in hexagonal prisms or in microscopic needles if the solution is rapidly cooled; it has m. p. 245—246° (Found: C, 81·6; H, 4·8; N, 4·3. $C_{23}H_{15}O_2N$ requires C, 81·9; H, 4·5; N, 4·2%). The base is moderately readily soluble in hot benzene or chloroform, very sparingly soluble in hot alcohol, and almost insoluble in ether or light petroleum. The red solution in sulphuric acid exhibits intense violet fluorescence, changing to blue fluorescence on dilution with water. Unlike the related methylenedioxyindenoquinoline (Part I, p. 831), this phenyl derivative is precipitated by the addition of water to its solution in glacial acetic acid. The *hydrochloride*, decomp. 247°, and the *picrate*, decomp. 236°, crystallise in yellow needles. The *methosulphate* separated in the course of 30 minutes from a boiling solution of the base (3 g.) and methyl sulphate (27 c.c.) in benzene (130 c.c.). The precipitate (3·8 g.) crystallised

from ethyl alcohol in pale yellow needles, m. p. 233° (Found: S, 7·0. $C_{25}H_{21}O_6NS$ requires S, 6·9%). The salt is moderately readily soluble in hot water and its aqueous and alcoholic solutions exhibit intense bluish-violet fluorescence. The *methiodide*, obtained directly or by double decomposition of the methosulphate, is sparingly soluble in water and alcohol and crystallises from the latter in small, pale yellow needles, m. p. 241—242° (decomp.).

Anhydro-7 : 8-*methylenedioxy*-11-*phenylindenoquinoline Methohydroxide* (V, VI).—On addition of aqueous potassium hydroxide (5 c.c. of 50%) to a hot solution of the preceding methosulphate (1 g.) in aqueous alcohol (80 c.c. of 50%), there was an immediate separation of pale green, very slender, microscopic needles. The mixture was boiled for 1 minute, filtered hot, and the residue well washed with hot alcohol and dried in a vacuum at 100° until its weight was constant (0·65 g.) (Found: C, 81·4; H, 5·0; N, 4·2. $C_{24}H_{17}O_2N$ requires C, 82·0; H, 4·8; N, 4·0%). The substance is readily soluble in chloroform to an emerald-green solution, and by careful addition of light petroleum it can be precipitated in small, green needles which darken at 226°, progressively decompose at higher temperatures, and finally melt to a black liquid at 246—247°. It is less readily soluble in benzene or toluene and undergoes decomposition in these media, which change is, however, no doubt due to oxidation. The base is slightly soluble in boiling water, the solution exhibiting bright blue fluorescence, and with acids the methosalts of the parent base are regenerated. The *picrate* crystallises in pale yellow needles which sinter at 221° and melt at 226°. The readily soluble *methiodide* of this anhydro-base is a pale yellow substance which gives an orange, amorphous precipitate with potassium hydroxide in aqueous solution. The new compound is easily soluble in cold water to a yellow fluorescent solution and is clearly a methohydroxide. It shows no tendency to give an anhydro-base and behaves exactly as would be anticipated if the methylation had proceeded so as to produce the group –CMePh–. A quite similar case was described in Part I (p. 834), and we are of the opinion that the analogy supports our view of the nature of the substance which is now under discussion. The green colour of the base may, however, be due to impurity.

3-*Methyl*-3-iso*carboline* (VII).—3-Carboline (Lawson, Perkin, and Robinson, J., 1924, **125**, 626), prepared by the improved method of Robinson and Thornley (*ibid.*, p. 2169), readily yields a *methosulphate* when its solution in hot nitrobenzene is treated with a solution of neutral methyl sulphate in toluene. The derivative is readily soluble in water and but sparingly soluble in alcohol, from which it crystallises in stellate clusters of pointed needles.

A concentrated aqueous solution was decomposed by an excess of warm 40% potassium hydroxide, and the base at once extracted by a large volume of light petroleum. The solution was dried with powdered potassium hydroxide and then with anhydrous barium oxide, filtered, and distilled with every precaution to avoid access of moist air. At a certain stage, crystallisation of the anhydro-base commenced and after cooling the small, yellow prisms, m. p. 140°, were collected (Found: in material dried at 95° in a high vacuum, C, 78·8; H, 5·6. $C_{12}H_{10}N_2$ requires C, 79·1; H, 5·5%).

The base is soluble in water, the solution being colourless and having an alkaline reaction. Aqueous acid solutions do not exhibit fluorescence. The base combines with methyl iodide to form a nearly colourless salt, which with silver oxide gives an alkaline, faintly fluorescent solution. The methohydroxide so obtained is precipitated by the addition of sodium hydroxide and exhibits no tendency to give an anhydro-base.

6′-Aminopiperonylideneoxindole (VIII).—Aqueous potassium hydroxide (8 c.c. of 60%) was added to a cold solution of oxindole (3 g.) and 6-aminopiperonal (3·2 g.) in methyl alcohol (40 c.c.). The precipitate of fine, orange needles which formed when the darkened liquid was stirred was washed with methyl alcohol, dried at 100°, and twice crystallised from ethyl alcohol to remove persistent inorganic contamination. The deep orange needles (3·1 g.) obtained decomposed at 226° (Found: C, 68·3; H, 4·7. $C_{16}H_{12}O_3N_2$ requires C, 68·6; H, 4·3%). The base is to some extent soluble in boiling water to an orange solution, it is freely soluble in acetic acid or nitrobenzene and sparingly soluble in benzene. The mineral acid salts are sparingly soluble, pale yellow, crystalline substances. The *picrate* crystallises from ethyl alcohol in deep yellow needles, which darken at 235° but do not melt at 300°. The orange solution in sulphuric acid is not fluorescent, but if the salts of the base are decomposed by alkali and the product is dissolved in sulphuric acid, the solution exhibits intense bluish-violet fluorescence, which is clearly due to the formation of methylenedioxyquinindoline. The diazo-solution from the base is pale yellow and gives a crimson coloration with alkaline β-naphthol. The *methosulphate* (*6′-methylaminopiperonylideneoxindole methyl hydrogen sulphate*) was obtained in the following manner. The base (1·5 g.) was dissolved in nitrobenzene (30 c.c.) and toluene (30 c.c.), a solution of neutral methyl sulphate in toluene (10 c.c. of 75%) added to the boiling mixture, and the lamp removed. The derivative, which separated in a few minutes as a flocculent precipitate of yellow needles, was crystallised from 50% alcohol, washed with ether, and dried at 120° (1·2 g.) (Found: S, 7·8. $C_{18}H_{18}O_7N_2S$ requires S, 7·9%). The salt darkens at 289°,

but does not melt at 300°. It is sparingly soluble in water or ethyl alcohol, but more readily soluble in a mixture of the two. The open-chain structure is indicated chiefly by the fact that the solution in sulphuric acid is not at once fluorescent, but on standing for a few minutes acquires a phenomenal bluish-violet fluorescence.

10 : 11-*Anhydro*-7 : 8-*methylenedioxyquinindoline* 10-*Methohydroxide* (IX).—The pale lemon-yellow needles that formed almost immediately when aqueous potassium hydroxide (10 c.c. of 60%) was added to the preceding methosulphate (1 g.) dissolved in boiling aqueous alcohol (80 c.c. of 50%) were crystallised from alcohol, in which they were moderately readily soluble, and dried in a vacuum at 120° (0·5 g.), the substance becoming deep orange whilst seeming to retain the crystalline structure (Found : C, 74·0; H, 4·5; N, 10·3. $C_{17}H_{12}O_2N_2$ requires C, 73·9; H, 4·4; N, 10·2%). This base, m. p. 244°, is relatively stable and can be sublimed when carefully heated. It dissolves in sulphuric acid, the solution exhibiting a beautiful bluish-violet fluorescence. The mineral acid salts and the picrate crystallise in yellow needles. On boiling with water, reversion to the methohydroxide of the quinindoline derivative was observed.

Py-N-*Methylphenyldiveratroisoharmyrine* (X).—A solution of phenyldiveratroharmyrine (3 g.) (Lawson, Perkin, and Robinson, *loc. cit.*) in benzene (100 c.c.) was boiled with neutral methyl sulphate (3 g.) for 5 minutes, and the orange-yellow, crystalline product was washed with benzene, crystallised from ethyl alcohol (in yellow needles), and dried at 120° (Found : C, 59·9; H, 5·2. $C_{27}H_{28}O_8N_2S$ requires C, 60·0; H, 5·2%). In alcoholic solution, this salt exhibits bright green fluorescence. Its yellow, aqueous solution was decomposed with sodium hydroxide, the scarlet precipitate washed with aqueous sodium hydroxide, dried in a vacuum, and dissolved in a considerable volume of hot benzene. This solution was dried with potassium hydroxide, and most of the solvent distilled, when the new base crystallised in bright scarlet, dense clusters of prismatic needles which darken above 140°, are chocolate at 240°, black at 260°, and melt at 264° with further decomposition (Found : in material dried at 110° in a high vacuum; C, 72·7; H, 5·7; N, 6·4. $C_{26}H_{24}O_4N_2$ requires C, 72·9; H, 5·6; N, 6·5%). The solution in neutral solvents such as ether or benzene has a fine violet fluorescence, but in alcohol or water the base gives a yellow solution with green fluorescence and has obviously reverted to phenyldiveratroharmyrine methohydroxide. Its yellow solution in sulphuric acid exhibits intense yellowish-green fluorescence and becomes deep ivy-green on heating. The base forms a *methiodide* which is sparingly soluble in ethyl alcohol and crystallises in slender, short, microscopic,

yellow needles, m. p. 266—267°. This salt exhibits green fluorescence in solution and gives no precipitate with ammonia or sodium carbonate in aqueous solution (solutions of the anhydro-base are so precipitated), whilst with sodium hydroxide in excess it gives a pale yellow precipitate of a stable methohydroxide, soluble in water.

(1 : 6)-*Naphthadiquinoline* (XII).—β-Naphthaquinoline was nitrated according to Claus and Besseler (*loc. cit.*), and the nitro-derivative reduced in the following manner: A solution of crystallised sodium sulphide (45 g.) in water (50 c.c.) was gradually added to a boiling solution of nitro-β-naphthaquinoline (16 g.) in aniline (100 c.c.), causing a vigorous reaction. The liquid was boiled for 30 minutes, the aniline distilled in steam, and the residue crystallised from 30% aqueous alcohol, 8 g. of amino-β-naphthaquinoline, m. p. 158°, being obtained. The diquinoline was obtained by the methods (A) and (B). (A) A mixture of amino-β-naphthaquinoline (13 g.), nitrobenzene (7·5 g.), sulphuric acid (20 g.) and glycerol (25 g.) was heated (oil-bath at 150—160°) during 6 hours. The base was rendered to ether (6 extractions), and the solution dried and concentrated to small bulk, when pale yellow needles (2·1 g.) slowly separated. The substance is sparingly soluble in ether, benzene, or alcohol (Found: C, 83·3; H, 4·6; N, 12·5. $C_{16}H_{10}N_2$ requires C, 83·5; H, 4·4; N, 12·2%).

(B) 5-Nitro-2-naphthylamine (3·4 g.) was gradually added to 60% acetic acid (60 c.c.) and iron filings (10 g.) at the temperature of the steam-bath. When the red colour had disappeared, water (100 c.c.) was added, and the solution was boiled for 5 minutes and filtered into dilute sulphuric acid (150 c.c. of 25%); the colourless needles of 1 : 6-naphthylenediamine sulphate obtained on cooling were dried (6·1 g.). A mixture of this sulphate (6 g.), nitrobenzene (4 g.), glycerol (16 g.), and sulphuric acid (16 g.) was heated (oil-bath at 155—165°) for 4·5 hours. The diquinoline was extracted from the solution, diluted and made strongly alkaline, by means of ether and 0·6 g. was ultimately obtained in colourless needles, by crystallisation from acetone. The substances prepared by methods (A) and (B) or a mixture of the two melted at 183·5—184·5°. Both specimens dissolve in dilute sulphuric acid, the colourless solutions exhibiting a bright blue fluorescence. The *sulphate* prepared from either of the specimens darkens above 250° and melts indistinctly at 268°.

5 : 6-(2 : 3-*Diphenylindolo*) (6 : 7)-*quinoline* (XIII).—An intimate mixture of amino-β-naphthaquinoline (7 g.), its dihydrochloride (3 g.), and benzoin (20 g.) was heated at 180—190° for 4 hours. The product was extracted by boiling benzene (150 c.c.) for 10 minutes, and the reddish-brown residue was separated from the hot

solution and triturated with aqueous potassium hydroxide. The isolated, washed, and dried product crystallised from nitrobenzene (50 c.c.) in colourless platelets (4 g.), which began to decompose at 298° (Found : C, 88·0; H, 5·0; N, 7·9. $C_{27}H_{18}N_2$ requires C, 87·6; H, 4·9; N, 7·6%). This base is very sparingly soluble in most organic solvents and forms very sparingly soluble, yellow salts with mineral acids. The solution in sulphuric acid exhibits green fluorescence which is persistent on dilution with water. When a trace of sodium nitrite or potassium dichromate is added to the sulphuric acid solution, an intense emerald-green coloration is developed. The *acetate* crystallises from glacial acetic acid in yellow needles decomposing above 300° (Found : C, 77·5; H, 5·4. $C_{27}H_{18}N_2,C_2H_4O_2,H_2O$ requires C, 77·7; H, 5·4%). A 75% solution (20 c.c.) of methyl sulphate in toluene was added to a boiling solution of the base (2 g.) in nitrobenzene (60 c.c.), the source of heat removed, the mixture cooled, ether added (200 c.c.), and the product (2·6 g.) crystallised from boiling alcohol, the *methosulphate* being obtained in intense yellow needles which become scarlet at about 165°; it is almost insoluble in boiling water (Found : S, 6·3. $C_{29}H_{24}O_4N_2S$ requires S, 6·5%). The decomposition of this methosulphate by alcoholic potassium hydroxide gave a crimson precipitate of microscopic needles, m. p. 225° (decomp.) if quickly heated, but we were unable to reach a definite conclusion in regard to the nature of the substance. It is reconverted by mineral acids into yellow, crystalline salts.

2 : 3-*Dimethoxyindophenazine* (XIV).—This substance was readily obtained by a slight modification of the method employed by Schunck and Marchlewski in the preparation of indophenazine (*Ber.*, 1895, **28**, 2528). 4 : 5-Dinitroveratrole (8 g.) was reduced in boiling acetic acid solution (200 c.c. of 50%) by the addition of zinc dust. When the colour changed from red to pale yellow, the solution was filtered and added to isatin (5 g.) dissolved in boiling acetic acid (125 c.c. of 20%). The yellow precipitate was collected after 5 minutes, washed with hot water, and dried at 150° (5·1 g.). The substance is readily soluble in hot nitrobenzene; it is sparingly soluble in boiling ethyl acetate or toluene, and separates from the latter in slender, yellow needles, m. p. 284° (Found : C, 68·8; H, 5·0; N, 15·1. $C_{16}H_{13}O_2N_3$ requires C, 68·8; H, 4·7; N, 15·0%). The neutral solutions have a violet-blue fluorescence and the cherry-red solution in sulphuric acid becomes deep purple on the addition of a trace of sodium nitrite or potassium dichromate. Mineral acid salts are bright yellow; the *hydrochloride*, m. p. 290° (decomp.), dissolves in water, the solution being yellow with green fluorescence, and in concentrated hydrochloric acid forming a blood-red solution.

The *picrate* crystallises from acetone in pale yellow needles, m. p. 254°. The *methosulphate* crystallised in large, flat, rectangular prisms on cooling a mixture obtained by the addition of a solution (100 c.c. of 75%) of methyl sulphate in toluene to a hot solution of the base (1·5 g.) in nitrobenzene (30 c.c.); a further quantity was precipitated by ether, the total yield being 2 g. The derivative crystallises from methyl alcohol in prisms, m. p. 247° (Found: S, 7·7. $C_{18}H_{19}O_6N_3S$ requires S, 7·9%). It is readily soluble in water, the solution exhibiting blue fluorescence, and is more sparingly soluble in alcohol.

2 : 3-*Dimethoxy*-5 (or 11)-*methyl*iso*indophenazine* (XV).—Potassium hydroxide (15 c.c. of 50%) was added to a boiling solution of the dimethoxyindophenazine methosulphate (2·7 g.) in 50% alcohol (60 c.c.). The deep red solution, on cooling, deposited voluminous, slender, scarlet needles which were washed with ether and dried at 120° (2·4 g.). The substance can be crystallised by careful addition of light petroleum to its benzene solution in scarlet needles sintering at 257° and melting at 261°, or from alcohol containing potassium hydroxide in scarlet prisms (Found: C, 69·3; H, 5·3; N, 14·4. $C_{17}H_{15}O_2N_3$ requires C, 69·6; H, 5·1; N, 14·3%). This base is moderately readily soluble in ethyl acetate or benzene, very readily soluble in chloroform, and sparingly soluble in ether. Like the parent dimethoxyindophenazine, it can be sublimed by careful heating in a tube. On boiling with water, an orange solution is obtained, and this becomes yellow after the addition of an acid. The *methiodide* crystallises in deep yellow needles, m. p. 205° (decomp.). If the dimethoxyindophenazine methosulphate is decomposed by potassium hydroxide in 50% alcohol in the cold, and the precipitate crystallised from the same solvent, slender, yellow needles, m. p. 278° (decomp.), of the *methohydroxide* are obtained (Found: C, 65·7; H, 5·2. $C_{17}H_{17}O_3N_3$ requires C, 65·6; H, 5·5%). This substance is moderately readily soluble in hot water, forming a yellow solution. *Dimethoxymethyl*iso*indophenazine dimethosulphate* was obtained when a mixture of the anhydro-base (1·5 g.), methyl sulphate (10 c.c. of a 75% solution in benzene), and benzene (50 c.c.) was boiled until the red colour had completely disappeared. The precipitated yellowish-green, microscopic needles were washed with ether and dried at 100° (1·5 g.). The substance is very readily soluble in water and somewhat readily soluble in alcohol, from which it crystallises in orange needles, m. p. 238° (Found: S, 11·6. $C_{21}H_{27}O_{10}N_3S_2$ requires S, 11·7%). The solutions of the salt exhibit green fluorescence.

2 : 3-*Dimethoxy*-6-*methylindophenazine* 11 (or 5)-*Methohydroxide* (XVI).—Aqueous potassium hydroxide (10 c.c. of 50%) was added

to a hot solution of the preceding dimethosulphate (1 g.) in 50% alcohol (40 c.c.), when a momentary darkening occurred, giving place almost at once to an orange-yellow colour. The hot filtered solution soon deposited glistening, yellowish-orange needles (0·6 g.) and after recrystallisation from alcohol the substance melted at 164° (Found: C, 66·3; H, 6·0; N, 13·2. $C_{18}H_{19}O_3N_3$ requires C, 66·4; H, 5·9; N, 12·9%). The same substance was obtained by decomposition of dimethoxydimethylindophenazonium iodide. It is readily soluble in benzene, chloroform, alcohol, or acetone, sparingly soluble in alcohol or ether, and insoluble in light petroleum. The orange-yellow solution in dilute acids exhibits green fluorescence and the yellow solution in sulphuric acid becomes red when gently heated. Curious results followed on an attempt to introduce a third methyl group into the molecule. The base (0·5 g.), m. p. 164°, was heated in boiling benzene solution (16 c.c.) with methyl sulphate (4 c.c. of 75% solution in benzene) for 10 minutes. The dark brown oil which separated solidified on scratching and was collected and decomposed by aqueous-alcoholic potassium hydroxide. The product crystallised from aqueous alcohol in nearly colourless, silky needles, m. p. 85° (0·27 g.) (Found: C, 66·2; H, 6·2%). The compound appears to be different from the initial isomeride. It is much more soluble than the latter (m. p. 164°) and has a lower m. p. Possibly a methyl group has migrated to a new position, a suggestion which is clearly free from theoretical difficulty.

7-*Methoxy*-4-*phenylflavylium Salts* (XIX).—Anhydro-7-hydroxy-2 : 4-diphenylbenzopyranol (1 : 4) (1·5 g.), methyl sulphate (15 c.c. of a 75% solution in benzene), and benzene (50 c.c.), all of which had been carefully dried, were mixed and the liquid was boiled until the red colour had changed to orange-yellow. On cooling, pale yellow, glistening needles separated, and these were washed with ether and dried (1·2 g.) (Found: S, 7·4. $C_{23}H_{20}O_6S$ requires S, 7·5%). This *methosulphate*, m. p. 179°, is readily soluble in alcohol, acetic acid, acetone, or hot dilute hydrochloric acid, forming yellow solutions which exhibit very intense bluish-green fluorescence. The salt is to some extent hydrolysed by water. Addition of ether to the original mother-liquor from the preparation precipitates a yellow, amorphous substance (S, 9·1%), which behaves in the same manner as the methosulphate with solvents and in the preparation of the ferrichloride. The latter, namely, 7-*methoxy*-4-*phenylflavylium ferrichloride*, was prepared in the usual manner and crystallised from acetic acid in feathery, yellow needles, m. p. 191° (Found: C, 51·8; H, 3·1. $C_{22}H_{17}O_2Cl_4Fe$ requires C, 51·7; H, 3·3%). The salt was prepared for comparison from 7-hydroxy-2 : 4-diphenylbenzopyranol dimethyl ether (Bülow and Sicherer, *Ber.*, 1901, **34**,

2380), and a mixture of the specimens melted at 190—191°. The m. p., 185°, previously given for this ferrichloride (Crabtree, Robinson, and Turner, J., 1918, **113**, 877) is too low. This substance gives a negative result in a Zeisel estimation, probably on account of the insolubility of the iodide, and after the addition of phenol the production of methyl iodide could be observed.

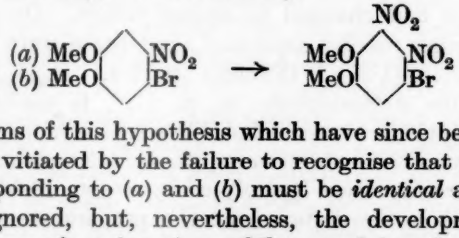
The authors' thanks are due to the Department of Scientific and Industrial Research for grants which enabled one of them (J. W. A.) to take part in the investigation.

THE UNIVERSITIES OF ST. ANDREWS AND MANCHESTER. [*Received, April 6th,* 1925.]

CCXII.—*The Nitration of* m-*Meconine.*

By JNANENDRA NATH RÂY and ROBERT ROBINSON.

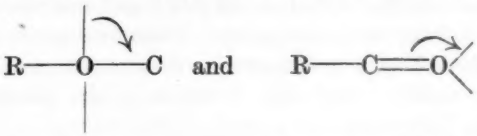
IN 1917 Jones and Robinson (J., **111**, 905) directed attention to a number of benzene substitution reactions which appeared to show that when two identical groups such as alkyloxy coexist in a molecule and direct substituents to different positions, the influence of the one which is in the *o*- or *p*-position to a negative * group is weakened so that the other alkyloxy- or similar group controls the direction taken by the reaction. For example, in the nitration of 4-bromo-5-nitroveratrole, the nitro-group diminishes the directive power of the methoxyl (*b*) in the *p*-position to a greater extent than that of (*a*) in the *m*-position and therefore the latter induces substitution, apparently abnormally, ortho to nitroxyl.



The criticisms of this hypothesis which have since been published have all been vitiated by the failure to recognise that the directing groups corresponding to (*a*) and (*b*) must be *identical* and therefore have been ignored, but, nevertheless, the development of the electronic theory of conjugation, whilst supplying the explanation of the phenomenon, also suggests a restriction to be placed on its scope. One of the most fundamental properties of oxygen and nitrogen, exhibited in carbon compounds, is expressed in terms of the electronic theory in the statement that bivalent oxygen and

* At the time, such groups as NO_2, CO_2H, SO_3H were called negative, and this is, of course, still permissible if the general polarity is the circumstance which ought to be emphasised.

tervalent nitrogen tend to increase the covalency at their single bindings, especially when attached to unsaturated systems, whereas there is a tendency to reduce the covalency of doubly linked oxygen or nitrogen. The free electrons on the oxygen and nitrogen are diminished in number in the former case and augmented in the latter. These changes are represented by the schemes:



In the first case, the oxygen becomes charged positively and in the second negatively. Now in the carbethoxyl and acid amide groups these tendencies can co-operate without disturbance of the octets and this is sufficient to explain the failure of the ester group to

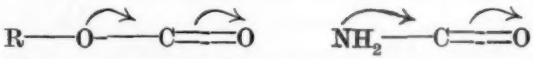


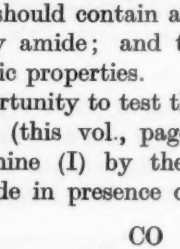
exhibit marked carbonyl reactivity and of the amide group to function as a strong basic centre. The positive charge on the carbon of the carbonyl group is neutralised from the chain and so does not seek foreign negative ions, whilst, in the amide group, the free electrons in the nitrogen octet are equally occupied in the chain to some extent; and it is these free electrons which impart the basic properties to ammonia. A similar neutralisation of the functions of groups like RO and C=O can occur if these are separated by an *even* number of unsaturated atoms (compare *Chemistry and Industry Review*, 1925, **44**, 18, 456), because in that case polarisation is possible without producing charges on intermediate atoms of the chain and without disturbing the octets.* We can therefore well understand the partial neutralisation of the directive power of methoxyl by a nitroxyl group situated in the *p*-position to it as shown in the annexed expression and, further, we suggest that the

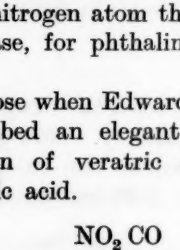
neutralisation considered by Jones and Robinson is always of this type. At present the effect can be predicted with confidence only when the directing group is derived from –OH, –NH_2, or –SH and

* We use the octet theory here, as always, in order to give a standard of numerical comparison. It does not affect the theory if the stable electronic configurations have more or less than 8 electrons, provided that the number tends to remain constant.

when the neutralising group is of the type $-NO_2$, –CO–R, etc. Certainly CO_2H is not such a group, being, as explained above, a self-contained assemblage. On the other hand, the carbonyl of phthalide is beyond doubt a more activating carbonyl than the carbonyl of an ordinary ester group. This is shown by condensation reactions of the methylene group in the ortho-position and on our theory means that the –CO–O– complex is not so completely satisfied in itself as it is in a typical ester. Therefore a similarly situated –CO–NH– should contain a more basic nitrogen atom than that of an ordinary amide; and this is the case, for phthalimidine has definite basic properties.

The opportunity to test this matter arose when Edwards, Perkin, and Stoyle (this vol., page 198) described an elegant synthesis of *m*-meconine (I) by the condensation of veratric acid with formaldehyde in presence of hydrochloric acid.

(I.) 



(II.)

As demanded by the theory which has been discussed above, this substance gives on nitration its 6-*nitro*-derivative (II), and we venture to suggest that such a result cannot be satisfactorily explained on any theory of the mechanism of aromatic substitution which is not based on electronic conceptions of valency. The constitution of (II) was proved by its conversion into a corresponding *bromo*-m-*meconine*, which is also obtained by applying the method of Edwards, Perkin, and Stoyle to 2-bromoveratric acid, the orientation of the groups in the molecule of which has been placed beyond question. Hope and Robinson (J., 1911, **99**, 1163) showed that phthalide contains a reactive $-CH_2-$, because it condenses with cotarnine to form anhydrocotarninephthalide. The poor yield was improved and became almost quantitative when a nitroxyl was introduced into the *o*- or *p*-position to the methylene group. The condensation is also facilitated, although to a less striking extent, when a nitroxyl group is introduced in the *m*-position to the methylene group (compare P., 1911, **27**, 229). A new example of this phenomenon is now forthcoming, since we are able to prepare *anhydrocotarnine-nitro*-m-*meconine* by a direct condensation of the components indicated.

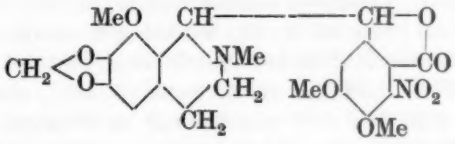
EXPERIMENTAL.

Preparation of m-*Meconine* (I).—The method of Edwards, Perkin, and Stoyle (*loc. cit.*) gives improved yields if the following slight

modification is adopted. A solution of veratric acid (50 g.) in hot acetic acid (250 c.c.) is, after the introduction of concentrated hydrochloric acid (200 c.c.) and aqueous formaldehyde (60 c.c. of 40%), heated on the steam-bath for 12 hours, cooled, tarry matter precipitated by the addition of a little water, and the brown liquid treated with charcoal, filtered, and concentrated in a vacuum to about one-fifth of its volume. Further tarry material is precipitated from the hot solution by addition of not too much water, and, after filtration, *m*-meconine is thrown down by further dilution with water and neutralisation with sodium carbonate. The *m*-meconine, crystallised from aqueous ethyl alcohol, has m. p. 155° and the yield averages 30 g.

6-*Nitro*-4 : 5-*dimethoxyphthalide* (II).—*m*-Meconine (13 g.) was gradually added with agitation to nitric acid (22 c.c.; *d* 1·42) at 0°; after a few hours the mixture was added to water, and the precipitate collected and extracted with boiling alcohol (30 c.c.). The residue crystallised from boiling acetic acid in colourless needles, m. p. 183—184° (yield 6—7 g.) (Found: C, 50·4; H, 3·4. $C_{10}H_9O_6N$ requires C, 50·2; H, 3·7%). This substance is sparingly soluble in hot alcohol and exhibits the behaviour of a lactone. Unlike nitromeconine, it does not give an intense coloration on treatment with hot alkaline solutions and this is clearly due to the fact that the methylene and nitroxyl groups are in the *m*-position to each other.

Anhydrocotarnine-6-*nitro*-4 : 5-*dimethoxyphthalide*,



—A mixture of nitro-*m*-meconine (3 g.), cotarnine (3 g.), and ethyl alcohol (300 c.c.) was boiled for 1·5 hours and then concentrated to one-fourth of its bulk and cooled. The crystalline deposit was isolated, treated with glacial acetic acid, and, after dilution with water and filtration, the base was precipitated by means of ammonia, collected, washed, and dried (2·5 g.). The base is very sparingly soluble in most neutral organic solvents and is best crystallised from boiling toluene–alcohol, from which it separates in well-defined, rectangular plates, m. p. 200° (decomp.) (Found: C, 57·8; H, 4·7, 4·8, 5·5; $C_{22}H_{22}O_9N_2$ requires C, 57·6; H, 4·8%). The base is readily soluble in dilute hydrochloric acid and acetic acid to a colourless solution. It is stable to hot dilute hydrochloric acid, but is gradually decomposed by boiling acetic acid with formation of cotarninium acetate

and nitro-*m*-meconine. It is, however, much more stable to hot acetic acid than anhydrocotarnine-nitromeconine; ease of formation and ease of decomposition going together in this series as in most others.

6-*Amino*-4 : 5-*dimethoxyphthalide*.—Nitro-*m*-meconine (11 g.) was gradually added to a hot solution of crystallised stannous chloride (35 g.) in concentrated hydrochloric acid (65 c.c.), when a clear liquid resulted, and the reaction was completed by heating on the steam-bath for 30 minutes. After dilution with water (250 c.c.) the cooled solution deposited crystals, which were isolated and treated with sodium bicarbonate in hot aqueous suspension. The substance crystallised from aqueous alcohol in colourless, feathery needles, m. p. 158° (yield about 6 g.) (Found: C, 57·0; H, 5·3. $C_{10}H_{11}O_4N$ requires C, 57·4; H, 5·3%). The amine is readily soluble in concentrated hydrochloric acid, but is precipitated on the addition of water. In suspension in dilute hydrochloric acid it can be diazotised, giving a bright yellow diazonium salt, which couples with β-naphthol to form a red azo-compound.

6-*Bromo*-4 : 5-*dimethoxyphthalide*.—(A) A solution of amino-*m*-meconine (6 g.) in 6% hydrochloric acid (60 c.c.) was diazotised at 0° and added to a solution of cuprous bromide (prepared from 2·4 g. of copper sulphate, potassium bromide and sulphur dioxide) in hydrobromic acid (4 c.c.; *d* 1·49). The reaction was completed by heating, and, after cooling, the precipitated solid was collected and crystallised from boiling water containing a little alcohol. The almost colourless, prismatic needles had m. p. 223°, alone or mixed with a specimen prepared by the following method.

(B) A mixture of 2-aminoveratric acid (7·1 g.) (Pschorr and Sumuleanu, *Ber.*, 1899, **32**, 3410), water (50 c.c.), and concentrated hydrochloric acid (10 c.c.) was treated at 0° with sodium nitrite (2·7 g. in water, 20 c.c.), the clear diazo-solution added to one of cuprous bromide (from 2·4 g. of copper sulphate) in hydrobromic acid (4 c.c.; *d* 1·49), and the reaction completed by heating on the steam-bath, evolution of nitrogen being first observed at 80°. The crude 2-bromoveratric acid which separated on cooling was crystallised from hot aqueous acetic acid and had m. p. 200° (yield 4—5 g.). Zincke and Francke (*Annalen*, 1896, **293**, 187) give m. p. 201°, their initial material being hemipinimide (compare Kühn, *Ber.*, 1895, **28**, 810).

A mixture of 2-bromoveratric acid (4 g.), aqueous formaldehyde (5·5 c.c. of 40%), concentrated hydrochloric acid (20 c.c.), and acetic acid (30 c.c.) was heated on the steam-bath during 10 hours. The product was added to water (250 c.c.), the precipitate of unchanged acid removed, and the filtrate concentrated to about 50 c.c. in a

vacuum and then neutralised with solid sodium bicarbonate. The solid which gradually separated crystallised from boiling water containing a little alcohol in colourless, prismatic needles, m. p. 223° (Found: C, 44·3; H, 3·1. $C_{10}H_9O_4Br$ requires C, 43·9; H, 3·3%).

THE UNIVERSITY, MANCHESTER. [*Received, May 13th*, 1925.]

CCXIII.—*The System Sodium Sulphite–Sodium Hydroxide–Water.*

By DALZIEL LLEWELLYN HAMMICK and JOHN ALEXANDER CURRIE.

A STUDY of this system was undertaken in order to find out the nature of the solid phases in equilibrium with solutions containing sodium sulphite and hydroxide. As our object was this, rather than the exact form of the solubility curve showing the amount of solids in solution, we did not aim at an accuracy of more than $\pm$ 0·5% in our analyses.

Sodium sulphite was prepared by passing sulphur dioxide into a solution of A.R. sodium carbonate (The British Drug Houses), precautions being taken throughout that air should not come into contact with the solution. Slightly more sulphur dioxide was passed in than would be sufficient to form the sulphite, in order to eliminate the danger of a double salt of sulphite and carbonate crystallising. Any hydrogen sulphite that might thus be formed would be turned into the normal salt when mixed with the soda solution in the solubility vessel. In practice, it was found that the normal salt came down under these conditions. The solution thus prepared was transferred, in contact with hydrogen only, to an electrically heated glass evaporator through which was passed a current of purified hydrogen. When a good crop of crystals had been deposited, the liquid was drained off, the crystals were washed and dried in an atmosphere of hydrogen, and stored in a vacuum desiccator over soda sticks.

The salt was tested for sulphate and rejected if any was found to be present. It was then analysed as sulphate, no specimen being used that had SO_3 lower than 63·2%, theory requiring 63·47%.

Sodium hydroxide. For the preparation of solutions up to 20% NaOH Cornog's method was used (*J. Amer. Chem. Soc.*, 1921, **43**, 2573). For stronger solutions we took advantage of the fact that from very strong solutions of sodium hydroxide nearly all the carbonate present is precipitated (Freeth, *Phil. Trans.*, 1922, **223**, 35). By allowing saturated solutions of the best soda sticks (The British

Drug Houses) to reach equilibrium at a temperature slightly above that of the isotherm we were studying, we obtained a solution of sodium hydroxide on filtering that was as strong as we required and that gave no precipitate with barium chloride solution. The suspensions complained of by Freeth were not observed, the solution being quite clear after filtering through Gooch asbestos.

Water. All water used in preparing the materials and making up solutions was distilled and then boiled under reduced pressure for ½ hour.

Solubility Determinations.—Complexes of approximately known composition were made up in one of two kinds of vessel. When the strength of the sodium hydroxide in solution did not exceed 25%, we used very wide test-tubes of Duro resistance glass closed by tight-fitting rubber stoppers through which a stirrer passed, fitted with a mercury seal. For stronger solutions, a silver vessel was employed similar to that used by Freeth (*loc. cit.*). Glycerol was used as a seal and lubricant, precautions being taken that none of it should leak into the solution.

The vessels were placed in an ordinary gas-regulated thermostat for the isotherms at 20°, 25°, and 32°, the temperature of which did not vary by more than $\pm 0{\cdot}1°$. For the isotherm at 0·15°, ice was placed in a well-lagged thermostat, and kept near the bottom with wire netting. The thermostat was then filled with water and kept well stirred; by this means and by renewing the ice every 48 hours the temperature never varied by more than 0·05°.

After equilibrium had been obtained—about 24 hours for weak solutions and 36—48 for strong ones was found to be sufficient—the contents of the vessel were rapidly transferred to a filter. This was so designed that the separation of the solution and moist solid could be carried out in the thermostat, a precaution found to be necessary when the soda content of the solution was either very weak or very strong. The whole operation was carried out as rapidly as possible.

Analysis.—After they had been weighed, the solutions and moist solids were made up in water to suitable volumes, portions of which were analysed. The sulphite was first oxidised to the sulphate by treatment with pure hydrogen peroxide solution and after standing a short time the excess of peroxide was decomposed by boiling. The sulphite was then estimated as barium sulphate and the hydroxide by titration, the water being obtained by difference. The results were plotted by the usual Schreinemakers method on a triangular diagram (see Figs. 1 and 2).

Results.—The isotherms at 0·15° and 32° are shown in the diagrams. The isotherms at 20° and 25°, being of the same general

form as that at 0·15°, have not been shown. The figures are given below. Compositions are given in weight per cent.

Isotherm at 0·15°.

Liquid.		Residue.		
NaOH.	Na_2SO_3.	NaOH.	Na_2SO_3.	Composition of solid phase in water.
—	12·2*	—	—	$Na_2SO_3,7H_2O$
3·0	9·0	0·8	43·9	,,
9·0	5·2	1·9	41·3	,,
16·9	2·8	2·4	44·5	,,
21·9	2·21	2·3	44·9	,,
23·3	2·2	3·7	55·3	$Na_2SO_3,7H_2O$ and Na_2SO_3
25·4	1·3	6·4	76·0	Na_2SO_3
26·6	0·7	3·6	87·5	,,
27·1	0·4	6·6	75·3	,,
27·9	0·1	—	—	,,
29·1	0·1	35·5	0·9	Na_2SO_3 and $NaOH,4H_2O$
29·5†	—	—	—	$NaOH,4H_2O$

Isotherm at 20°.

—	21·2*	—	—	$Na_2SO_3,7H_2O$
1·6	18·7	0·3	47·4	,,
4·4	15·4	—	—	,,
8·3	12·0	—	—	,,
9·9	11·0	3·3	37·4	,,
11·6	9·9	—	—	,,
12·2	9·6	—	—	,,
12·7	9·4	—	—	,,
13·4	9·2	—	—	,,
14·0	9·0	0·2	68·3	$Na_2SO_3,7H_2O$ and Na_2SO_3
13·8	8·6	1·1	77·4	,, ,,
15·5	7·0	1·0	95·5	Na_2SO_3
16·0	6·7	3·8	87·0	,,
20·2	3·5	—	—	,,
24·9	1·1	—	—	,,
26·8	1·0	—	—	,,
36·3	0·1	5·6	85·2	,,
50·1	Trace	8·3	82·1	,,
52·2†	—	—	—	$NaOH,H_2O$

Isotherm at 25°.

—	23·6*	—	—	$Na_2SO_3,7H_2O$
0·7	22·5	—	—	,,
2·5	19·3	0·3	48·4	,,
5·0	17·7	0·8	47·1	,,
9·7	13·0	1·7	42·1	,,
9·8	13·2	0·1	56·3	$Na_2SO_3,7H_2O$ and Na_2SO_3
9·6	13·8	0·7	92·8	,, ,,
12·2	10·2	0·5	95·1	Na_2SO_3
12·6	10·1	—	—	,,
14·2	8·2	—	—	,,
17·2	5·8	—	—	,,
20·7	2·9	2·9	86·8	,,
20·7	2·5	—	—	,,
25·2	1·0	—	—	,,
28·7	0·5	—	—	,,
29·4	0·3	—	—	,,
42·7	0·1	—	—	,,
43·9	Trace	—	—	,,
53·3†	—	—	—	$NaOH,H_2O$

* Lewis and Rivett, J., 1924, **125**, 1156. † Pickering, J., 1893, **63**, 890.

Isotherm at 32°.

Liquid.		Residue.		Composition of solid phase in water.
NaOH.	Na_2SO_3.	NaOH.	Na_2SO_3.	
—	26·5*	—	—	Na_2SO_3
0·6	26·4	—	—	,,
2·3	23·1	0·1	89·0	,,
5·1	19·1	0·1	89·0	,,
7·6	15·7	—	—	,,
11·1	11·2	0·8	93·6	,,
16·5	5·4	0·8	95·4	,,
20·1	2·9	2·1	90·5	,,
27·2	0·6	2·3	92·0	,,
36·2	0·1	6·0	83·1	,,
51·8	0·001	9·0	81·6	,,
54·4†	—	—	—	$NaOH,H_2O$

* Lewis and Rivett, J., 1924, **125**, 1156. † Pickering, J., 1893, **63**, 890

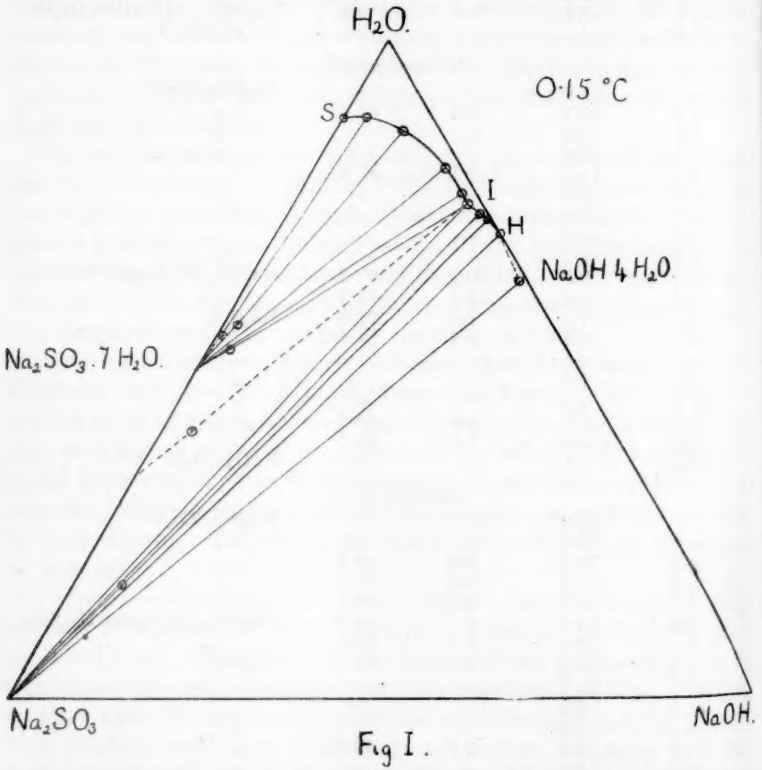


Fig I.

The isotherm at 0·15° is shown in Fig. I. The results obtained at 20° and at 25° give curves resembling Fig. I except that the heterogeneous region $Na_2SO_3,7H_2O$–S–I becomes smaller; in this region complexes separate into solutions of concentrations along S-I and sodium sulphite heptahydrate. Solutions of compositions given by I–H are in equilibrium with anhydrous sodium sulphite. The

point H, which lies very close to the side H_2O–NaOH (the solubility of sulphite being very small in excess of sodium hydroxide) represents the composition of the liquid in equilibrium with anhydrous sodium sulphite and sodium hydroxide tetrahydrate. Similar points were not realised experimentally at the other temperatures.

The isotherm at 32·0° (Fig. II) shows that at that temperature sodium sulphite heptahydrate cannot exist in contact with any aqueous solution. This is in accordance with the results obtained by Lewis and Rivett (J., 1924, **125**, 1156), who found the transition

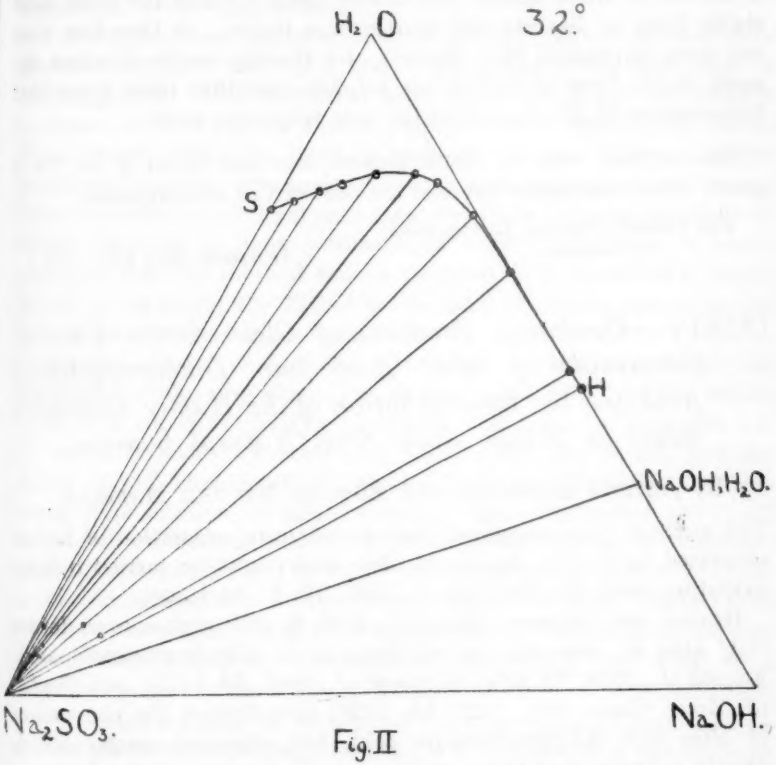


Fig. II

point between anhydrous and hydrated sodium sulphite to lie at 31·5°. The fact that heptahydrate appeared as a solid phase in the isotherm at 25° is in conflict with the result obtained by Hartley and Barrett (J., 1909, **95**, 1178), who record 22° as the transition point. Recently, however, Foerster, Brosche, and Norberg-Schulz (*Z. physikal. Chem.*, 1924, **110**, 450), as the result both of solubility measurements and dilatometer experiments, have concluded that the transition point lies at 33·4°.

The above discrepancies seem at first sight hard to reconcile.

Lewis and Rivett (*loc. cit.*) have, however, established the fact that anhydrous sulphite may exist in more than one metastable solid phase, particularly in the presence of sodium sulphate, which appears in solid solution in the sulphite crystals. Different solid phases in equilibrium would readily account for the comparatively small difference between the transition point found by Foerster and by Lewis and Rivett. Moreover, the latter workers record (*loc. cit.*, p. 1166) a temperature of 39° as the transition point between one form of anhydrous sulphite and the hydrated form; this temperature is almost as much above Rivett and Lewis's value for their most stable form as Barrett and Hartley's is below. It therefore does not seem impossible that Barrett and Hartley really obtained the most stable form of anhydrous sulphite and that their transition temperature of 22° represents the true transition point.

The authors wish to thank Messrs. Brunner Mond & Co. for a grant which has partly covered the cost of this investigation.

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CCXIV.—*Oxidation Products of Oleic Acid. Part I. Conversion of Oleic Acid into Dihydroxystearic Acid and the Determination of the Higher Saturated Acids in Mixed Acids from Natural Sources.*

By ARTHUR LAPWORTH and EDWARD NEVILLE MOTTRAM.

THE authors have suggested that an accurate estimation of higher saturated acids in a sample of oleic acid might be carried out by oxidation methods (*Biochem. J.*, 1925, **19**, 17, footnote).

Hazura and Grüssner (*Monatsh.*, 1888, **8**, 180) were able to detect oleic acid in mixtures by oxidising it to dihydroxystearic acid. Edmed (J., 1898, **73**, 627), Le Sueur (J., 1901, **79**, 1313), and Nicolet (*J. Amer. Chem. Soc.*, 1922, **44**, 1139) investigated the conversion of oleic into dihydroxystearic acid, but obtained results which clearly indicate that their experiments were not made under very favourable conditions. Edmed (*loc. cit.*) stated that practically quantitative yields of the dihydroxy-acid can sometimes be obtained, but unfortunately gave no clue to the necessary conditions.

Robinson and Robinson (this vol., p. 177) obtained excellent yields of the dihydroxy-acid by oxidising in dilute alkaline solution at 0°. Based on that observation, privately communicated some three years ago, a long series of systematic experiments has been carried out by the present authors and it is now possible to state

that the conditions essential for the nearly perfect conversion of oleic acid into dihydroxystearic acid are: (1) a low temperature (0—10°) during the oxidation process; (2) a concentration of oleic acid (in the form of its sodium or potassium salt) not exceeding 0·1%; (3) a concentration of the added aqueous permanganate solution not exceeding 1%; (4) a very short period of reaction, 5 minutes being sufficient for oxidation of nearly the whole of the oleic acid present; * (5) a slight excess of alkali should be present from the beginning of the oxidation, otherwise there is a danger of hydroxyketostearic acid being formed.

The observations can be applied to the analysis of comparatively impure samples of oleic acid, and in particular to the estimation of the proportion of all saturated fatty acids which are not volatile in steam, as, for example, stearic, palmitic and myristic acids. Even when much linolic or linolenic acid is present, their oxidation products (namely tetrahydroxy- and hexahydroxy-stearic acids) being insoluble in cold light petroleum and their degradation products either insoluble in light petroleum or volatile in steam, it seems probable that the method can be modified so as to afford a simple means of isolating the higher saturated fatty acids present in the mixed acids from many natural sources.

Detailed Analytical Method.†—The clear solution of sodium salts obtained by warming about 5 g. of the "oleic acid" on the water-bath with an equal weight of caustic soda, dissolved in 500 c.c. of water, is cooled, 4 litres of ice-cold water are added, and the whole is well shaken at 10° while 400 c.c. of 1% potassium permanganate solution are added quickly. After 5 minutes, the liquid is decolorised with sulphur dioxide, and concentrated hydrochloric acid (150 c.c.) added. The white, flocculent precipitate (A) of crude solid dihydroxystearic acid is drained for a short time, washed with about 50 c.c. of light petroleum (this greatly accelerates its subsequent drying: the petroleum washings are reserved),‡ and dried to a constant weight at the ordinary temperature in a vacuum desiccator.

* It is not desirable to submit the resulting dihydroxystearic acid to further action of the permanganate, and if it is desired to obtain the most precise results, a further conversion of the very small quantity of unchanged oleic acid is necessary and it is best to proceed as hereinafter described. For many purposes the results obtained by omission of the second oxidation process would be accurate enough.

† The solubility of dihydroxystearic acid in petroleum (b. p. 80—100°) is not more than 0·002 g. in 100 c.c. at 15°, and therefore negligible in applying this method.

‡ The aqueous filtrate contains no appreciable quantities of higher fatty acids, but does contain about 0·15 g. of products of lower molecular weight, such as nonoic, octoic, azelaic and suberic acids, formed by breaking down of a small fraction of the dihydroxystearic acid.

It is now extracted with 100—150 c.c. of warm light petroleum (b. p. about 70—80°), the whole cooled, filtered, and the residue (B) of nearly pure dihydroxystearic acid washed with several successive quantities of cold solvent. The petroleum extracts and washings are united and evaporated.*

The residue left on evaporation of the petroleum extracts is distilled with steam to remove traces of volatile fatty acids, and treated with low-boiling petroleum. This readily extracts the non-volatile acids, which, after evaporation of the solvent, are heated on the water-bath until constant in weight. On cooling, the residue (D) sets to a waxy solid and represents the higher saturated fatty acids present in the original sample of " oleic acid." †

Examples.—(1) A sample of oleic acid, O_1, was isolated from olive oil and purified through the barium salt (Lapworth and Mottram, *loc. cit.*). Its " first setting-point " (*loc. cit.*) was 12·55° and a break in the setting-point curve of its mixtures with pure palmitic acid took place with 4·7% of added palmitic acid. As the break corresponds with a total percentage $7{\cdot}2 \pm 0{\cdot}5$ of palmitic acid, O_1 consisted of $97{\cdot}5 \pm 0{\cdot}5\%$ of oleic acid and $2{\cdot}5 \pm 0{\cdot}5\%$ of palmitic acid.

Results of analyses by the above method : (*a*) 4·97 g. and (*b*) 3·06 g. of O_1 gave 0·1 g. and 0·07 g., respectively, of higher saturated acids, or 2·0 and 2·25%.

These three results agree very satisfactorily with one another. The weight of dihydroxystearic acid, free from fatty acids, obtained in (*a*) was 5·23 g. or 96% of the calculated amount (5·45 g.) from the 4·87 g. of pure oleic acid present. In case (*b*) the weight was again 95—96% of the calculated quantity. The loss of 4% was in part accounted for by the presence of 0·09 g. of azaleic (or suberic) acid, which, in case (*a*), was actually isolated from the aqueous filtrate and had evidently arisen by further oxidation of part of the dihydroxystearic acid.

* In order to effect, if desired, a complete conversion of the small quantity of oleic acid which still remains, the residue left on evaporation of the petroleum is oxidised as described above : 50 c.c. of cold $N/10$-sodium hydroxide and 100 c.c. of ice water; 15 c.c. of 1% potassium permanganate solution; 10 c.c. of concentrated hydrochloric acid. The precipitate (C) is washed with water, dried at the ordinary temperature, and extracted with cold light petroleum; about 0·05 g. of dihydroxystearic acid remains on the filter.

† " Non-saponifiable " constituents in the original sample are not, in the authors' experience, to be found in the residue (D), at least not in appreciable quantity. If thought desirable, however, the quantity of such constituents can easily be determined by the usual method, or perhaps more simply by dissolving the residue (D) in a little methyl alcohol, adding excess of methyl-alcoholic barium hydroxide, evaporating to complete dryness, and extracting the residue with dry acetone, in which barium hydroxide and barium salts of saturated fatty acids are insoluble.

The "saturated fatty acid," as isolated, melted at 57°, and doubtless consisted mainly of palmitic acid (m. p. 62·5°).

(2) *Total mixed acids from olive oil.* Olive oil was completely hydrolysed and the resulting mixed acids (O_2) were isolated. These had an iodine number = 88 and contained 1·4% of "unsaponifiable matter."

5·0 G. of O_2, treated as above described, gave 0·78 g. of higher saturated fatty acids (waxy, pale yellow solid, m. p. 53—54°) or 15·6%. On the assumption, then, that O_2 contained only the following constituents, its composition was roughly: Oleic acid, 72; linolic acid, 12—13; unsaponifiable matter, 1·4; higher saturated acids, 14—15%.* The total weight of dihydroxystearic acid isolated was 4·1 g. This doubtless contained tetrahydroxystearic acid arising from the linolic acid present, and other experiments have shown it to be purely fortuitous that this weight again represents 96% of the weight of dihydroxystearic acid theoretically obtainable from the oleic acid estimated as present in the mixed acids.†

The "unsaponifiable matter" in the 0·78 g. of higher saturated fatty acids, determined by the methyl-alcoholic baryta method (footnote, p. 1630), was a negligible quantity (only 0·02 g.).

(3) A sample of a commercial product sold as "pure oleic acid" yielded 16% of solid saturated fatty acids; but the weight of "dihydroxystearic acid" was very appreciably less (only 3·4 g. from 5 g.) than in the case of example (2). The manipulations offered no greater difficulties than in the previous cases.

The work described in the present paper was begun under the auspices of the Oils and Fats Committee of the Food Investigation Board. A grant from the Department of Scientific and Industrial Research to one of us (E. N. M.) rendered it possible for him to take part in the research and is gratefully acknowledged.

THE UNIVERSITY, MANCHESTER. [*Received, May 5th,* 1925.]

* The main object of the experiment was to ascertain whether the presence of so much linolic acid would affect the ease of filtration of the crude hydroxystearic acid, and from this point of view the results were all that could be desired. It now seems probable that estimates formed by previous workers of the proportion of oleic acid in the mixed acids from olive oil have been decidedly too high and those of the saturated fatty acids too low. This conclusion is also consistent with the experience which the writers had previously had in analyses of fractions of lead salts made in purifying oleic acid.

† Judging from the results of experiments which the authors have made on the production of hydroxyketostearic acid, the yield of dihydroxystearic acid may fall off very rapidly if the proportion of acids more highly unsaturated than oleic acid exceeds a certain maximum.

CCXV.—*The Action of Hydrogen Peroxide on Limonene.*

By JAMES SWORD.

THE oxidation of limonene with hydrogen peroxide (2 mols.) in acetic acid solution gives $\Delta^{8(10)}$-*p*-menthene-1 : 2-diol as the main product, a small yield of terpin hydrate, an aldehyde, etc. Larger quantities of the oxidising agent produce a variety of oxygenated compounds and resinous substances.

Since hydrogen peroxide has no action on hydrocarbons of the terpene series in solvents such as ether, it would appear that acetic acid takes a real part in the reaction, possibly by the formation of peracetic acid. This is supported by the fact that the reaction proceeds more quickly the larger the quantity of solvent used; a certain minimum amount is necessary for the reaction to go to completion in any length of time.

EXPERIMENTAL.

The limonene used was obtained from oil of bitter orange (J., 1907, **91**, 1872) and had b. p. 175·5—176·5°, $[\alpha]_D^{15°}$ + 96·89°, $d^{15°}$ 0·8453, $n^{15°}$ 1·4759.

100 C.c. of it in glacial acetic acid (375 c.c.) were shaken continuously for 14—18 days with perhydrol, added gradually (total 180 c.c.). The solution was neutralised with sodium carbonate, and extracted with ether, on occasions up to 40 times. The extract on concentration deposited about 1 g. of terpin hydrate, m. p. 116—117° (in a sealed tube) (Found: C, 62·8; H, 11·5%), and on evaporation left an oil, which was hydrolysed with methyl-alcoholic barium hydroxide, yielding an oil (*a*). This, on distilling under reduced pressure, gave three fractions: (i) a mobile oil, b. p. 110—112°/10 mm., (ii) the main fraction, a viscous oil, b. p. 140—143°/10 mm., from which a glycol (*b*) was isolated, (iii) a semi-vitreous solid, b. p. 150—152°/10 mm. These were all unsaturated, the unsaturation decreasing with increase of boiling point, and gave sodium derivatives [Found: for (i), Na, 9·5; for (ii), Na, 22·7; for (iii), Na, 16·1. $C_{10}H_{16}(ONa)_2$ requires Na, 21·3%. $C_{10}H_{17}\cdot ONa$ requires Na, 13·0%].

By using the residual oil from the preparation of the sodium compounds (only a small quantity of sodium was used for a relatively large amount of oil) the glycol (*b*) was finally induced to crystallise. Thereafter it could be crystallised directly from (*a*). The residual oil after its removal yielded a small quantity of a *p*-nitrobenzoate, m. p. 79°, gave with ethereal hydrogen bromide a dihydrobromide which crystallised from ethyl alcohol in pearly plates, m. p. 44—45° (Found: Br, 53·5. $C_{10}H_{16},2HBr$ requires

Br, 53·6%), and on distillation with steam yielded an unsaturated oil (Found: C, 72·0; H, 9·9%. 0·1818 G. absorbed 0·165 g. of bromine), from which no nitrobenzoate was obtained, and no solid on hydration.

The glycol (*b*) is soluble in about 10 parts of water and much more soluble in alcohol or ether. It will crystallise only when hydrated. The hydrate is efflorescent and contains three molecules of water, all of which can be removed over sulphuric acid in a vacuum desiccator in the course of 4—5 days. If dried too rapidly, it liquefies and then sets to a hard, vitreous solid. This, in conjunction with the fact that the hydrate has no definite melting point but begins to melt about 20° below the melting point of the anhydrous substance, indicates that there is an intermediate hydrate of lower melting point. Its solution in alcohol is optically inactive. The anhydrous substance is snow-white, melts sharply at 67·5°, and is clearly the $\Delta^{8(10)}$-*p*-menthene-1 : 2-diol described by Prileschaev (*Ber.*, 1909, **42**, 4814) (Found: C, 70·6; H, 10·5. Calc., C, 70·6; H, 10·7%).

From the original oxidation products a small quantity of an acid was isolated by means of its silver salt [Found: Ag, 55·4. $C_6H_{12}(CO_2Ag)_2$ requires Ag, 55·7%.]

The author wishes to acknowledge his indebtedness to Professor G. G. Henderson for his interest in the work.

THE UNIVERSITY OF GLASGOW. [*Received, April 28th*, 1925.]

CCXVI.—*Hydroxybenzils.*

By JOHN THOMPSON MARSH and HENRY STEPHEN.

SCHÖNBERG and his collaborators (*Ber.*, 1922, **55**, 1174, 3746, 3753) have shown that the oxidation of benzoins gives rise to benzils of two types, *viz.*, yellow compounds of the normal type, having the α-diketonic structure and characteristic properties, and colourless ψ-benzils, to which Schönberg ascribes a peroxidic structure which accounts for their slight reactivity towards the usual ketonic reagents.

Up to the present, few examples of colourless benzils were known (compare Irvine, J., 1907, **91**, 541; Vörlander, *Ber.*, 1911, **44**, 2455; Schönberg and Kraemer, *loc. cit.*, p. 1174; Schönberg and Malchow, *loc. cit.*, p. 3748) and only in one case, 4 : 4′-dibenzyloxybenzil, has the coloured diketone been converted into the colourless peroxide (Schönberg and Bleyberg, *loc. cit.*, p. 3753), and the latter, by

crystallisation from various solvents, reconverted into the coloured benzil. Schönberg therefore regards the two forms as being in equilibrium both in solution and at the melting point:

$$RO\cdot C_6H_4\cdot C(=O)\text{—}C(=O)\cdot C_6H_4\cdot OR \rightleftharpoons RO\cdot C_6H_4\cdot C(-O)=C(-O)\cdot C_6H_4\cdot OR.$$

By applying Hoesch's method of synthesising aromatic hydroxyketones (*Ber.*, 1915, **48**, 1122) to acyl cyanides and resorcinol and phloroglucinol, we have prepared the eight following colourless hydroxybenzils; the colours produced when they are dissolved in concentrated sulphuric acid are recorded:

2 : 4-Dihydroxybenzil, $C_6H_3(HO)_2\cdot CO\cdot COPh$, red.
2 : 4-Dihydroxy-2′-methoxybenzil, $C_6H_3(HO)_2\cdot CO\cdot CO\cdot C_6H_4\cdot OMe$, greenish-brown.
2 : 4-Dihydroxy-4′-methoxybenzil, $C_6H_3(HO)_2\cdot CO\cdot CO\cdot C_6H_4\cdot OMe$, purple.
2 : 4-Dihydroxy-3′ : 4′ : 5′-trimethoxybenzil, $C_6H_3(HO)_2\cdot CO\cdot CO\cdot C_6H_2(OMe)_3$, blue.
2 : 4 : 6-Trihydroxybenzil, $C_6H_2(HO)_3\cdot CO\cdot COPh$, red.
2 : 4 : 6-Trihydroxy-2′-methoxybenzil, $C_6H_2(HO)_3\cdot CO\cdot CO\cdot C_6H_4\cdot OMe$, reddish-brown.
2 : 4 : 6-Trihydroxy-4′-methoxybenzil, $C_6H_2(HO)_3\cdot CO\cdot CO\cdot C_6H_4\cdot OMe$, purple.
2 : 4 : 6-Trihydroxy-3′ : 4′ : 5′-trimethoxybenzil, $C_6H_2(HO)_3\cdot CO\cdot CO\cdot C_6H_2(OMe)_3$, greenish-blue.

With the exception of the last, these compounds darken before melting with decomposition. This change is not due to conversion of peroxide into diketone, for the acetyl derivatives remain colourless above their melting points.

The hydroxybenzils crystallise from dilute alcohol or dilute acetic acid in colourless needles. Their pink solutions in aqueous sodium hydroxide, on warming, become deep red, and on acidification the benzils are precipitated as bright yellow needles, from which the colour does not completely disappear on crystallisation; the melting points, however, are identical with those of the colourless forms. We have so far not obtained a pure, stable, coloured form of the above colourless benzils.

On account of the action of the alkali, methylation of the hydroxybenzils was not successful. Attempts to demethylate those compounds containing methoxy-groups did not give very satisfactory results.

The trihydroxybenzils give a purple coloration with ferric chloride solution, but only a faint colour was noticed with the dihydroxy-compounds. Both di- and tri-hydroxybenzils reduce Fehling's solution.

The solutions of the hydroxybenzils in organic solvents are colourless even on boiling and are stable towards hydroxylamine, phenylhydrazine, *p*-nitrophenylhydrazine, semicarbazide, and *o*-phenylenediamine, and the hydroxybenzils do not undergo the benzilic acid transformation.

From these facts, the authors are of the opinion that these

compounds are peroxides both in the crystalline form and in solution.

Experimental.

Preparation of Acyl Cyanides.—The following method differs in certain details from that suggested by Claisen (*Ber.*, 1898, **31**, 1023) and utilised by Mauthner (*Ber.*, 1908, **41**, 921; 1909, **42**, 189) and is of general application. It is a great improvement on the method of heating acid chlorides with cyanides of heavy metals.

A solution of the acid chloride (1 mol.) and pure hydrogen cyanide (4 mols.) in dry ether (5 vols.) was cooled in ice while anhydrous pyridine (4 mols.) was added gradually during 1 hour, and the mixture kept in ice-water for 12 hours. The pyridine hydrochloride was removed by filtration, and the ether and excess of pyridine by distillation, the latter under diminished pressure, and the residue of cyanide, having been freed from traces of pyridine hydrochloride by filtration in ethereal solution, was either distilled or crystallised.

This method avoids treatment with water and thereby eliminates any possibility of hydrolysis of the cyanide, to which the majority of the acyl cyanides are prone. In the cases investigated, the cyanides were usually sufficiently pure for condensation after evaporation of the ether. The yields are good.

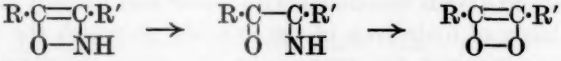
Benzoyl cyanide crystallises in pale yellow needles, m. p. 32°, from ligroin (compare Wöhler and Liebig, *Annalen*, 1832, **3**, 267).

o-Methoxybenzoyl Cyanide.—To prepare the requisite chloride, *o*-methoxybenzoic acid (1 mol.) was dissolved in thionyl chloride (1½ mols.) and the solution subsequently warmed on the water-bath for ½ hour; the excess of thionyl chloride was removed under diminished pressure, and the acid chloride distilled; b. p. 136°/12 mm. The duration of heating should not be longer than that stated, since thionyl chloride tends to demethylate the acid chloride. The same remarks apply to the preparation of *p*-methoxy- and 3 : 4 : 5-trimethoxy-benzoyl chlorides. Phosphorus pentachloride may be used in place of thionyl chloride, but gives poorer yields. *o-Methoxybenzoyl cyanide* crystallises from ligroin in long, yellow needles, m p. 56°, b. p. 161°/12 mm. (Found: C, 67·15; H, 4·2. $C_9H_7O_2N$ requires C, 67·1; H, 4·35%). It is readily soluble in most organic solvents and is rapidly hydrolysed by water.

p-Methoxybenzoyl cyanide has m. p. 63—64°, b. p. 150°/12 mm., and 3 : 4 : 5-trimethoxybenzoyl cyanide, m. p. 136—137° (compare Mauthner, *loc. cit.*). *Cinnamoyl cyanide*, m. p. 114—115°, was made by the acylation of hydrogen cyanide for the first time (compare Claisen and Moritz, *Ber.*, 1880, **13**, 2124).

Preparation of Benzils.—Dry hydrogen chloride was passed

rapidly for 2½ hours into a solution of the acyl cyanide (1 mol.) and resorcinol (or phloroglucinol) (1·1 mols.) in dry ether. *p*-Methoxy- and 3 : 4 : 5-trimethoxy-benzoyl cyanides, which are sparingly soluble in ether, were dissolved in chloroform and added to the ethereal solution of resorcinol (or phloroglucinol). The presence of chloroform hastened the deposition of the ketimine salt. The solution, which in every case turned red, was kept in ice for 3 days. The deposited ketimine hydrochloride was washed with ether, dissolved in just sufficient water, and the solution warmed to 60° and treated with sodium acetate, which precipitated the white, crystalline ketimine. This was readily soluble in dilute hydrochloric and sulphuric acids, the latter solution depositing a crystalline sulphate, generated ammonia when gently warmed with dilute aqueous sodium hydroxide, and was converted into the colourless benzil by boiling aqueous sodium acetate, the golden-brown colour of the solution soon fading to pale yellow. The following changes therefore probably occur during the hydrolysis:



Aqueous solutions of the ketimine hydrochlorides required several hours' warming on the water-bath before hydrolysis was complete.

2 : 4-*Dihydroxybenzil* has m. p. 239°, turning reddish-brown at about 234° (Found: C, 69·8; H, 4·2. $C_{14}H_{10}O_4$ requires C, 69·4; H, 4·1%).

2 : 4-Dihydroxybenzil was described by Finzi (*Monatsh.*, 1905, **26**, 1128) as a brown, amorphous substance, m. p. 239°. We were unable to make the dioxime and repetition of Finzi's experiment for the preparation of its hydrochloride failed to give the result he stated.

2 : 4-*Diacetoxybenzil* was prepared by boiling a solution of the benzil in acetic anhydride for 4 hours and pouring it into water, when the acetyl compound separated as a thick, pasty mass which soon solidified. It crystallised from alcohol in colourless needles, m. p. 159° (Found: C, 66·5; H, 4·4. $C_{18}H_{14}O_6$ requires C, 66·25; H, 4·3%).

The same method was employed for the preparation of the acetyl derivatives of the other benzils.

2 : 4-*Dihydroxy-2′-methoxybenzil* has m. p. 223° after darkening at about 210° (Found: C, 66·3; H, 4·5. $C_{15}H_{12}O_5$ requires C, 66·2; H, 4·4%). The *diacetyl* derivative has m. p. 144° (Found: C, 64·4; H, 4·7. $C_{19}H_{16}O_7$ requires C, 64·1; H, 4·5%).

2:4-*Dihydroxy*-4′-*methoxybenzil* has m. p. 234° after darkening at about 225° (Found: C, 66·3; H, 4·6%), and the *diacetyl* derivative has m. p. 178·5° (Found: C, 64·3; H, 4·6%).

2:4-*Dihydroxy*-3′:4′:5′-*trimethoxybenzil* has m. p. 257° after turning pink at 175°, yellow at 200°, and darkening at about 245° (Found: C, 61·6; H, 5·0. $C_{17}H_{16}O_7$ requires C, 61·45; H, 4·8%). The *diacetyl* derivative has m. p. 155° (Found: C, 60·3; H, 4·7. $C_{21}H_{20}O_9$ requires C, 60·6; H, 4·8%).

2:4:6-*Trihydroxybenzil* has m. p. 287° after darkening at about 260° (Found: C, 65·2; H, 4·2. $C_{14}H_{10}O_5$ requires C, 65·1; H, 3·9%). The *triacetyl* derivative has m. p. 248° (Found: C, 62·6; H, 4·4. $C_{20}H_{16}O_8$ requires C, 62·5; H, 4·2%).

2:4:6-*Trihydroxy*-2′-*methoxybenzil* has m. p. 235° after darkening at about 200° (Found: C, 62·8; H, 4·3. $C_{15}H_{12}O_6$ requires C, 62·5; H, 4·2%). 2:4:6-*Triacetoxy*-2′-*methoxybenzil* has m. p. 135°.

2:4:6-*Trihydroxy*-4′-*methoxybenzil* has m. p. 262° after darkening at about 250° (Found: C, 62·7; H, 4·2%). Its *triacetyl* derivative has m. p. 241° (Found: C, 61·0; H, 4·4. $C_{21}H_{18}O_9$ requires C, 60·8; H, 4·3%).

2:4:6-*Trihydroxy*-3′:4′:5′-*trimethoxybenzil* has m. p. 187° (Found: C, 58·6; H, 4·8. $C_{17}H_{16}O_8$ requires C, 58·7; H, 4·6%). The *triacetyl* derivative has m. p. 258° (Found: C, 58·1; H, 4·4. $C_{23}H_{22}O_{11}$ requires C, 58·3; H, 4·6%).

The triacetoxybenzils are only moderately soluble in alcohol and were crystallised from alcohol–acetic acid.

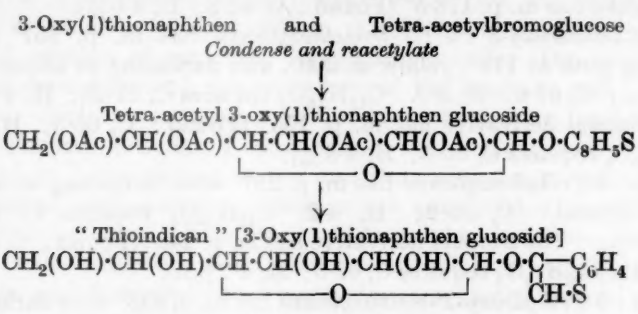
THE UNIVERSITY, MANCHESTER. [*Received, May 1st*, 1925.]

CCXVII.—*Studies of the Glucosides. Part III. The Synthesis of "Thioindican."*

By JAMES CRAIK and ALEXANDER KILLEN MACBETH.

MACBETH and PRYDE (J., 1922, **121**, 1660) deduced the constitution of indican from a study of the hydrolytic products of the methylated glucoside, and hoped to synthesise the glucoside itself through the condensation of tetra-acetylbromoglucose and derivatives of indoxyl. From preliminary attempts it would appear that indoxyl in relatively large amounts is necessary for successful condensation. In view of the difficulty in obtaining sufficient quantities of this material, and of the ease with which it oxidises, it was decided to standardise the experimental methods by examining the conditions in the case of the condensation of tetra-acetylbromoglucose and 3-oxy(1)thionaphthen.

The work described in this paper is outlined in the following scheme:



EXPERIMENTAL.

Tetra-acetylbromoglucose is most conveniently prepared in small quantities by a method devised in the St. Andrews Laboratories. Acetyl bromide (40 g.) is added to anhydrous glucose (10 g.) in a flask immersed in cold water and attached to a reflux condenser. After about 10 minutes a vigorous reaction sets in and the glucose has all dissolved in about ½ hour. The product is poured into ice-water (300 c.c.), and the resulting solid twice washed with sodium bicarbonate solution and then with water until free from acid. The dried ethereal solution of the residue is concentrated greatly, and the addition of light petroleum precipitates an oil which solidifies within 12 hours. Rapid recrystallisation from amyl alcohol gives a pure white, crystalline product which keeps for several months in a desiccator over soda–lime or calcium chloride (yield 10—12 g.).

3-Oxy(1)thionaphthen was prepared by Smiles and McClelland's method (J., 1921, **119**, 1813). We obtained better yields by keeping the temperature at 40—45° during the initial condensation of the 2-thiolbenzoic acid and ethyl acetoacetate and allowing the reaction to continue for about 2 hours.

Condensation of Tetra-acetylbromoglucose and 3-Oxy(1)thionaphthen.—Attempts to effect the condensation in ethereal solution by shaking with silver oxide gave a product containing a considerable quantity of " thioindigo," from which none of the tetra-acetyl glucoside could be isolated. The best results were obtained by heating tetra-acetylbromoglucose (25 g.) and 3-oxy(1)thionaphthen (13 g.) with quinoline (10 g.) for about 2 hours at 105—110° in an atmosphere of carbon dioxide. The product was poured into ice-water (300 c.c.), extracted with ether, and the extract was washed free from quinoline with *N*-sulphuric acid, then with sodium

bicarbonate solution and water until free from acid. After evaporation of the ether, a rapid steam distillation removed the excess of oxythionaphthen. Thereafter the water was distilled off under reduced pressure, and the dry residual syrup reacetylated by acetic anhydride (60 c.c.) and pyridine (60 c.c.). The crude tetra-acetyl glucoside was obtained by pouring the acetylation mixture into ice-water and ether and washing as described above. The red syrupy residue from the ethereal extract was dissolved in hot alcohol (150 c.c.), and hot water carefully added until turbidity was just appearing. The brown solid obtained on standing yielded in the best experiments about 2·5 g. of white needles, m. p. 106°, of the *tetra-acetyl glucoside* after repeated crystallisation from 60% alcohol. The glucoside is insoluble in water but soluble in the usual organic solvents. In acetone it has $[\alpha]_D + 7{\cdot}4°$ (Found: C, 54·7; H, 4·8; S, 6·7. $C_{22}H_{24}O_{10}S$ requires C, 55·0; H, 5·0; S, 6·7%).

In some experiments, the product obtained was a dark syrup which could not be crystallised even after reacetylation. It contained no bromine, did not reduce Fehling's solution, and analysis showed it to consist essentially of the tetra-acetyl glucoside; and on deacetylation it yielded the parent glucoside.

Deacetylation of the Tetra-acetyl Glucoside.—(a) *With barium hydroxide.* Barium hydroxide (45 c.c. of 0·174 *N*-solution) was added to a hot solution of the tetra-acetyl glucoside (0·8268 g.) in alcohol (40 c.c.). After some minutes barium was precipitated by a stream of carbon dioxide, and the carbonate filtered and washed with alcohol. The united filtrates on evaporation under diminished pressure gave a red syrup, which was extracted with boiling alcohol, and hot water added to the filtrate till turbidity was just appearing. On cooling, "*thioindican*" (I) separated as a mass of fine, glistening needles, coloured pink by traces of "thioindigo." Recrystallised with the aid of a little norit, it gave a pure white product (0·15 g.), m. p. 73·5°, which behaved as a glucoside and did not reduce Fehling's solution until after hydrolysis. It was soluble in alcohol or acetone, and insoluble in ether, light petroleum, or water. The rotation, showing a low dextro-value, was too small at the low concentration available to give a trustworthy reading (Found: C, 53·6; H, 5·3. $C_{14}H_{16}O_6S$ requires C, 53·8; H, 5·1%).

(b) *Alcoholic ammonia.* In this more satisfactory method, the tetra-acetyl glucoside (0·8 g.) was dissolved in a solution of dry ammonia in absolute alcohol. After 10 hours the greater part of the ammonia was removed by a current of air, and the residual solution evaporated under diminished pressure at a bath temperature of 20°. Acetamide was removed by extracting the product

six times with water (10 c.c.), and the residue crystallised as described in (a). Yield 0·13 g. (25% of the theoretical).

Since the red syrup already referred to proved to be essentially glucosidic, it was subjected to hydrolysis as described above. Acetamide and other impurities were removed by repeated extraction with ether. Addition of light petroleum to a concentrated alcoholic solution of the residue precipitated a red solid which on repeated crystallisation from aqueous alcohol yielded fine, white needles of the parent glucoside, m. p. 73·5°.

Estimation of the oxythionaphthen content of the glucoside by simultaneous hydrolysis and condensation with isatin in aqueous hydrochloric acid solution according to the method for estimating indican in plant extracts (Orchardson, Wood, and Bloxam, *J. Soc. Chem. Ind.*, 1907, **26**, 4) gave results which were much too low even when the acid concentration was considerably increased and the time of refluxing greatly extended. The characteristic red condensation product was obtained in a yield of only 48%, the low m. p. of the glucoside and its insolubility in water being doubtless the cause. The estimation may, however, be carried out satisfactorily in alcoholic solution. A solution of "thioindican" (0·0405 g.) in alcohol (100 c.c.) containing isatin (0·23 g.) and concentrated hydrochloric acid (20 c.c.), when boiled under reflux for 10 hours, gave 0·0364 g. of the red condensation product ($C_{16}H_9O_2N_2S$). Theory requires 0·0362 g.

We are indebted to the Department of Scientific and Industrial Research for a grant which enabled one of us (J. C.) to participate in the work.

THE UNIVERSITY, ST. ANDREWS.
THE UNIVERSITY, DURHAM. [*Received, May 14th*, 1925.]

CCXVIII.—*Echitamine.*

By JOHN AUGUSTUS GOODSON and THOMAS ANDERSON HENRY.

THE alkaloid echitamine was first prepared by Gorup-Besanez (*Annalen*, 1875, **176**, 88) from the bark of *Alstonia scholaris*, R.Br. (*Echites scholaris*, L.) and was the subject of much controversy between O. Hesse (*Annalen*, 1875, **176**, 326; **178**, 49 (with Jobst); 1880, **203**, 144; *Ber.*, 1880, **13**, 1841) and Harnack (*Arch. exp. Path. Pharm.*, 1877, **7**, 126; *Ber.*, 1878, **11**, 2004; 1880, **13**, 1648) in the course of which it was shown that Harnack's ditaine (derived from "dita bark," a native name for the bark of *A. scholaris*) is identical with echitamine. Hesse's observations on the alkaloid

were largely confirmed by Bacon (*Philippine J. Sci.*, 1906, **1**, 1007). The position arrived at may be summarised thus: *A. scholaris* bark contains at least two alkaloids: (*a*) ditamine, amorphous, isolated by extracting with ether the residue from an alcoholic extract of the bark, rendered alkaline with ammonia, and (*b*) echitamine (ditaine), obtained by extraction of the same residue, rendered alkaline with solution of sodium or potassium hydroxide, with chloroform, after the removal of ditamine. It is clear from this preliminary work that echitamine is a strong base which, unlike ditamine, cannot be liberated from its salts by ammonia, and the separation of the two alkaloids is based on this fact. The first description of echitamine was given by Hesse (*Annalen*, 1880, **203**, 144), who stated that the free base (echitammonium hydroxide) formed glassy prisms, $C_{22}H_{30}O_5N_2,3H_2O$, m. p. 206°, $[\alpha]_D^{15°} - 28{\cdot}8°$ in alcohol, lost $3H_2O$ at 80° and a fourth molecule of water at 105° in a vacuum, forming a new base, $C_{22}H_{28}O_4N_2$, weaker than the original, but yielding the same hydrochloride, $C_{22}H_{28}O_4N_2,HCl$. Harnack, on the contrary, assigned the formula $C_{22}H_{30}O_4N_2,HCl$ to the hydrochloride.

In addition to *A. scholaris*, several other species of *Alstonia* have been examined. Hesse found in *A. constricta* the amorphous bases porphyrine and chlorogenine (subsequently renamed alstonine) and the crystalline alkaloid, alstonidine (*Annalen*, 1865, Suppl. IV, p. 40; 1880, **205**, 360; *Ber.*, 1878, **11**, 1546. Compare von Muller and Rummel, J., 1879, **35**, 31; Oberlin and Schlagdenhauffen, *J. Pharm.*, 1879, **28**, 576). From a Java species, *A. spectabilis*, R. Brown, Hesse obtained echitamine, ditamine and two other alkaloids, echitenine and alstonamine, the last-named substance being crystalline (*Ber.*, 1878, **11**, 1546; *Annalen*, 1880, **203**, 170), but could find no trace of Scharlec's alstonine (*Genees. Tijd. Ned. Ind.*, 1863, **10**, 209).

Much work has also been done on the sterols and other crystalline, non-nitrogenous substances of Alstonia species. Jobst and Hesse found in *A. scholaris* bark, echikautschin (amorphous); echicerin, $C_{30}H_{48}O_2$, m. p. 157°, $[\alpha]_D + 63{\cdot}75°$; echitin, $C_{32}H_{52}O_2$, m. p. 170°, $[\alpha]_D + 75{\cdot}25°$; echitein, $C_{42}H_{70}O_2$, m. p. 195°, $[\alpha]_D + 85{\cdot}4°$, and echiretin, $C_{35}H_{56}O_2$ (amorphous).

From the dried latex of *Alstonia costulata*, Miq. (*Dyera costulata*, Hook) Sack and Tollens isolated a similar series of sterols (*Ber.*, 1904, **37**, 4110), which Cohen (*Arch. Pharm.*, 1907, **245**, 236) subsequently identified with lupeol, and α- and β-amyrins, and Ultée (*Chem. Weekblad*, 1914, **11**, 456) found the same three constituents in the latex of *A. scholaris*.

The material used in the present investigation consisted of bark

derived from *A. congensis*, Engler. The first sample was collected in the Cameroons by Dr. Lehmann, and for it and the supplies subsequently received from the Cameroons, the Conservator of Forests, Gold Coast, and the Director of Forests, Nigeria, the authors are indebted to the kindness of Dr. Hill, Director of the Royal Botanic Gardens, Kew.

The results of the present investigation confirm Hesse's empirical formula for echitamine, and many of the unexplained points recorded by Hesse and Harnack in the course of their controversy as to the formula of echitamine are accounted for by the fact now established that echitamine is a methyl ester and is hydrolysed with great ease, forming the new base *demethylechitamine*, $C_{21}H_{26}O_4N_2$. It is also shown that echitamine contains a methylimino-group, but whether this has a tertiary or secondary nitrogen is uncertain, as the alkaloid appears to yield a crystalline nitroso-derivative. For the same reason, it is uncertain whether one or two hydroxyl groups are present, as the second acetyl group in the diacetylechitamine now described may indicate the presence of either a hydroxyl group or a secondary nitrogen atom.

Finally, the fact that the parent alkaloid and all the derivatives described give an intense blue colour with Hopkin and Cole's glyoxylic reagent for tryptophan (*Proc. Roy. Soc.*, 1901, **68**, 21) must be taken to mean that echitamine has an indole nucleus, and support for this view is given by the production of an indole-like base, as one product, when echitamine is distilled with alkalis.

A. congensis bark, like other barks of this genus, contains much amorphous alkaloid in addition to echitamine and yields a large quantity of non-nitrogenous products. Of the latter, one substance, a well-crystallised lactone, $C_9H_{14}O_3$, was isolated as a by-product in the purification of echitamine and has been characterised. It is converted by sodium hydroxide into a crystalline sodium salt, $C_9H_{15}O_4Na$, and yields a monoacetyl derivative, so that its formula may be extended thus, $HO\cdot\overline{C_8H_{15}CO\cdot O}$.

For some of the echitamine used in this investigation the authors are indebted to Prof. F. L. Pyman, F.R.S., who isolated it from the bark of another species, *A. Gillettii*, kindly supplied by Fr. Just. Gillet, Curator of the Botanic Gardens, Kisanti, Belgian Congo.

The various Alstonia barks are used in the localities where they occur, as remedies for malaria, but so far no attempt has been made to use echitamine in medicine. The authors are indebted to Dr. J. Trevan of the Wellcome Physiological Research Laboratories for the observation that echitamine hydrochloride is toxic to mice

in doses of 0·3 to 0·5 mg. per 20 g. and that it acts by paralysis of the medulla.

In connexion with the use of the bark in malaria Major Brown of the Wellcome Bureau of Scientific Research found that the hydrochloride was not toxic to protozoa (Glaucoma) at a concentration of 0·03%, but became so at a concentration of 0·0025% in presence of *N*/800-alkali (compare Bacon, *loc. cit.*).

Experimental.

The finely-ground bark (1 kg.) was exhausted with hot alcohol, the concentrated solution poured into warm 1% acetic acid (500 c.c.), and the filtrate from this concentrated to 200 c.c. After agitation with ether (extract A) and chloroform (extract B) in turn to remove wax and other impurities, the liquor was rendered alkaline with sodium hydroxide solution and the liberated alkaloids were dissolved out with chloroform. The residue from the chloroformic solution was dissolved in alcohol, and the liquid rendered slightly acid with hydrochloric acid (10%) and set aside. Echitamine hydrochloride gradually crystallised and was collected, washed with a little alcohol, and recrystallised from water. The yield of crystalline hydrochloride from different samples of *A. congensis* bark varied considerably.

	Gold Coast.	Nigeria.	Cameroons.
Total alkaloid %	0·38 to 0·56	0·11 to 0·12	0·18
Echitamine hydrochloride %	0·18 to 0·34	0·03 to 0·04	0·09

As few data are recorded by previous workers regarding the base and its salts, the opportunity has been taken to characterise these substances.

The hydrochloride obtained was identical with echitamine hydrochloride from *A. scholaris* bark. When crystallised quickly from water, it forms long, anhydrous needles, m. p. 295° (corr.; decomp.), $[\alpha]_D^{15°}$ − 58° (in water; $c = 1\%$) (Found : C, 62·6, 62·9; H, 7·1, 7·1; N, 6·4; Cl, 8·4, 8·5. $C_{22}H_{28}O_4N_2$, HCl requires C, 62·8; H, 6·9; N, 6·9; Cl, 8·4%). When crystallised slowly from water, it forms stumpy prisms, m. p. 292° (corr.; decomp.), $[\alpha]_D^{15°}$ − 54·3° ($c = 1·028$; water) (Found : loss at 100° in a vacuum, 4·79. Calc. for $C_{22}H_{28}O_4N_2$,HCl,H_2O : H_2O, 4·15%). Both forms of the hydrochloride are neutral to litmus. Hesse (*loc. cit.*) records for his hydrochloride $C_{22}H_{28}O_4N_2$,HCl, $[\alpha]_D$ − 57° ($c = 2$; water). The hydrobromide, similarly obtained, forms transparent prisms, m. p. 258° (air-dry; corr.; decomp.), 268° (dry; corr.; decomp.), $[\alpha]_D^{15°}$ − 43·5° for the hydrated salt ($c = 0·804$ in water) (Found : C, 56·4; H, 6·5; Br, 16·9. Calc. for $C_{22}H_{28}O_4N_2$,HBr : C, 56·8; H, 6·3; Br, 17·2%. Loss on drying at 105° in a vacuum, 3·7. Calc. for $C_{22}H_{28}O_4N_2$,HBr,H_2O :

H_2O, 3·7%). Hesse gives the formula $C_{22}H_{28}O_4N_2,HBr,2H_2O$ to his hydrobromide.

The hydriodide, similarly prepared, crystallises from water in long, anhydrous prisms, m. p. 267° (corr.; decomp.) (Found: C, 51·4; H, 5·9; I, 24·0. Calc. for $C_{22}H_{28}O_4N_2,HI$: C, 51·6; H, 5·7; I, 24·8%).

The sulphate is more soluble than the halide salts, separates only after considerable concentration of the neutralised solution, and is best recrystallised by adding alcohol to a strong solution of the salt in water. It forms rosettes of needles, which decompose from 275° onwards; $[\alpha]_D^{15°}$ — 51·6° (c = 2·58 in water) [Found for air-dry salt: loss at 100° in a vacuum, 2·4. $(C_{22}H_{28}O_4N_2)_2,H_2SO_4,H_2O$ requires H_2O, 2·04%. Found in dry salt: H_2SO_4, 11·46. Calc., H_2SO_4, 11·31%].

The *nitrate*, obtained by neutralising the base in chloroform with N/10-nitric acid, separates, on cooling the concentrated aqueous solution, in elongated pyramids, $C_{22}H_{28}O_4N_2,HNO_3,2H_2O$, m. p. 127° (air-dry; corr.; decomp.), 176° (dry; corr.), $[\alpha]_D^{15°}$ — 51·4° (air-dry salt in water; c = 1·01) (Found: loss on drying in a vacuum over sulphuric acid, 8·15. Calc., 7·45%. Found in dry salt: C, 58·9; H, 6·8. Calc., C, 59·0; H, 6·5%).

The neutral oxalate, $(C_{22}H_{28}O_4N_2)_2,H_2C_2O_4$, was only obtained as a gelatinous precipitate, although Hesse (*loc. cit.*) obtained it crystalline (Found: C, 63·9; H, 6·7. Calc., C, 64·3; H, 6·8%). When the calculated quantity of oxalic acid is added to a solution of the base in alcohol, the neutral oxalate first formed dissolves and on adding a little water and removing the alcohol by distillation in a vacuum, rosettes of needles of *echitamine hydrogen oxalate*, $C_{22}H_{28}O_4N_2,H_2C_2O_4,2H_2O$, m. p. 238° (corr.; decomp.), separate on cooling (Found: loss on drying at 100° in a vacuum, 6·3. Calc., H_2O, 7·05%. Found in dry salt: C, 61·0; H, 7·0. Calc., C, 60·7; H, 6·4%).

The picrate is precipitated when picric acid solution is added to the hydrochloride dissolved in water. The air-dry substance softens at 50°, decomposes at 98°, and loses in a vacuum at atmospheric temperature over sulphuric acid 41·3%, corresponding to $24H_2O$. On recrystallisation from dilute alcohol it forms minute rosettes of needles, $C_{22}H_{28}O_4N_2,C_6H_2(OH)(NO_2)_3,2H_2O$, which behave like the air-dry substance on heating (Found: loss on drying in a vacuum over sulphuric acid, 5·5. Calc., 5·6%. Found in dry substance: C, 54·6; H, 5·1. Calc., C, 54·8; H, 5·1%).

Determinations of methoxyl and methylimino-groups by the usual methods on the hydrochloride and hydriodide gave the following results. Hydrochloride: Found; MeO, 7·2; NMe, 7·6. Calc.

for MeO, 7·4; NMe, 6·9%. Hydriodide: Found; MeO, 6·0, 6·1; NMe, 6·0. Calc. for MeO, 6·1; NMe, 5·7%.

Diacetylechitamine Hydrochloride.—Echitamine hydrochloride was mixed with a few drops of pyridine and heated at 100° with six parts by weight of acetic anhydride. On cooling, the diacetyl derivative separated in silky masses of needles and more was obtained by concentrating under reduced pressure. After recrystallisation from ethyl acetate the substance had m. p. 271° (corr.; decomp.) [Found in substance dried at 105° in a vacuum: C, 61·7; H, 6·7; Cl, 6·8; MeO, 6·6; acetic acid (by hydrolysis with phosphoric acid), 26·2. $C_{22}H_{26}O_4N_2Ac_2,HCl$ requires C, 61·8; H, 6·6; Cl, 7·0; MeO, 6·2; acetic acid, 23·8%].

Hydrolysis of Echitamine.—The base used in preparing the salts described above was obtained by dissolving the hydrochloride, as isolated (p. 1643), in water, adding sodium hydroxide, and extracting with chloroform. If complete removal of this solvent by distillation is attempted, the base decomposes as already recorded by Hesse (*Annalen*, 1880, **203**, 144), who called the product oxyechitamine and gave it the formula $C_{22}H_{28}O_5N_2$. The change is probably more profound than Hesse supposed, but the substance has not been examined in the course of this work. The solvent can, however, be largely removed by distillation and the residue, dissolved in alcohol, used for the preparation of salts, but it has not been possible to induce the base to crystallise, though Hesse, as already stated, obtained a base which he at one time regarded as a crystalline tetrahydrate, $C_{22}H_{28}O_4N_2,4H_2O$. In the course of attempts to crystallise the base, water was added (after some days) to a solution in alcohol, prepared as described, and on long standing this deposited crystalline material, more of which was slowly obtained by continued dilution with water.

The same substance was produced more rapidly by heating echitamine hydrochloride in sealed tubes at 120° during 6 hours with 0·24*N*-sodium hydroxide solution (20 c.c. per g. of hydrochloride). It can be recrystallised from hot 70% alcohol and then forms prisms or hexagonal plates, m. p. 290° (air-dry; corr.; decomp.) or 268° (dry; corr.; decomp.). It is sparingly soluble in alcohol, chloroform, or water and is neutral to litmus. It forms a *hydrochloride* crystallising in prisms from hot water, m. p. 306° (corr.; decomp.), which is acid to litmus and much less soluble in water (1 in 209, approx.) than echitamine hydrochloride (1 in 76 approx.) (Found for air-dry base: C, 62·2; H, 7·5; loss in a vacuum at 130°, 8·7. $C_{21}H_{26}O_4N_2,2H_2O$ requires C, 62·0; H, 7·4; H_2O, 8·9%. Found for base dried at 130° in a vacuum: C, 68·0, 68·3; H, 7·3, 7·3; N, 7·8. $C_{21}H_{26}O_4N_2$ requires C, 68·1; H, 7·1; N, 7·6%.

Found for hydrochloride, dried at 100° in a vacuum: C, 62·1, 62·2; H, 6·8, 6·8; Cl, 8·7. Calc. for $C_{21}H_{26}O_4N_2$,HCl: C, 62·0; H, 6·7; Cl, 8·7%).

These analyses indicate that the new base contains $-CH_2$ less than echitamine, and determinations showed that it still contained a methylimino-group but had lost the methoxyl group of echitamine (Found for air-dry base: MeO, 0; NMe, 7·1. $C_{21}H_{26}O_4N_2$ requires NMe, 7·8%. Found for dry hydrochloride: MeO, 0; NMe, 6·8. $C_{21}H_{26}O_4N_2$,HCl requires NMe, 7·1%). The new base is therefore called *demethylechitamine* and all its reactions indicate that the methyl group has been lost from a carbomethoxy-group. This assumption accounts for the neutrality to litmus of demethylechitamine and the acidity to litmus of the hydrochloride, echitamine being strongly alkaline and its hydrochloride neutral to this indicator. The new base, like echitamine and all its salts, gives an intense blue coloration with Hopkin and Cole's glyoxylic reagent for tryptophan.

Action of Nitric Acid on Echitamine.—Harnack stated (*Ber.*, 1878, **11**, 2004) that a carmine-red base was produced by the action of concentrated nitric acid on echitamine, but the substance was not analysed or further described. When nitric acid (18 c.c.) is added to echitamine nitrate (3·19 g.) in water (180 c.c.) and the solution is warmed at 100°, it becomes red, then green, and finally yellow. When sodium hydroxide solution is added to the cooled liquid, a red base is precipitated; and a little more can be recovered by extraction with chloroform. A solution of the red base in dilute alcohol on concentration and standing deposits rosettes of minute needles (yield 1·4 g.), but the bulk of it remains amorphous. After recrystallisation the air-dry base began to decompose at 156° and after drying at 105° in a vacuum showed shrinkage at 163° (corr.) and frothed at 184° (corr.). It is almost insoluble in water, forms a red solution in alcohol and in chloroform a yellow solution with a red fluorescence [Found in air-dry base: loss at 105° in a vacuum, 12·1. $C_{22}H_{26}O_4N_2(NO_2)_2,4H_2O$ requires H_2O, 13·2%. Found in base dried at 105° in a vacuum: C, 55·6; H, 6·0; N, 11·6. Calc.: C, 55·7; H, 5·5; N, 11·8%].

The red base still contains intact the methoxyl group of echitamine (Found in dry base: MeO, 6·9. Calc., 6·5%).

The red colour is sharply changed to yellow on neutralisation with acid, and on adding standard alkali to a solution of a known weight of the base in a known excess of standard acid a sharp end-point is reached when a slight permanent red precipitate is formed. A molecular-weight determination by this method gave 474 [Calc. for $C_{22}H_{26}O_4N_2(NO_2)_2$, *M*, 489]. The red base appears therefore to be a simple dinitro-derivative of echitamine, but the change is

probably more far-reaching than is indicated by the empirical formula.

On treatment with sodium nitrite and dilute hydrochloric acid at 0°, echitamine gives a small yield (8%) of a substance crystallising from ether in rosettes of yellow needles, which shrinks at 140° and melts at 157° (decomp.) and, as it gives Liebermann's reaction, is probably a nitroso-derivative.

Distillation of Echitamine with Alkalis.—When echitamine is heated dry with soda-lime or with an aqueous solution of potassium hydroxide (50%), an alkaline, aqueous distillate is obtained when the temperature is kept below 250°. On neutralisation with hydrochloric acid and redistillation, this affords a distillate which when poured on a hot, oxidised copper spiral yields formaldehyde, due to the presence of methyl alcohol liberated by the hydrolysis of the carbomethoxy-group already referred to (p. 1646). The aqueous liquor in the distillation flask, on evaporation to dryness, left a small quantity of a hydrochloride.

The distillation was continued up to 310° and finally under reduced pressure until nothing more came over. The distillates thus obtained were acidified and extracted with ether, which removed 0·68 g. (from 8·6 g. of alkaloid) of an oil, having a pronounced fæcal odour. This oil gave a red coloration with Ehrlich's reagent, an orange colour with Nelson's solution, and dyed a pine splint, moistened with hydrochloric acid, red. It appeared therefore to be an indole derivative, but no well-defined product could be obtained from it. The acid mother-liquor was rendered alkaline and again extracted with ether, which removed 0·3 g. of a base from which also no crystalline derivatives could be obtained. The alkaline mother-liquor was then distilled, the distillate collected in dilute hydrochloric acid, and the salt produced isolated by the addition of alcohol to the highly concentrated liquor. The crystalline hydrochloride so obtained contained 52·5% of chlorine (Calc. for $CH_3{\cdot}NH_2,HCl$: Cl, 52·5%).

The products of this distillation are therefore methyl alcohol, methylamine, an indole derivative, and a third base.

Non-alkaloidal Constituents.

Isolation of a Lactone, $C_9H_{14}O_3$.—No attempt has been made to isolate the components of the waxy and other materials removed in extracts A and B (p. 1642) in the purification of the acetic acid solution, but as these materials retained some alkaloid they were extracted with dilute hydrochloric acid, which was then rendered alkaline with ammonia and re-extracted with chloroform. In this way a crystalline, nitrogen-free product was isolated, more of which

was obtained from the mother-liquors remaining from the separation of crude echitamine hydrochloride. The total yield amounted to 0·02% by weight of the bark used. No evidence has been obtained that this substance is a decomposition product of echitamine. It crystallises from hot water in colourless prisms or long needles, m. p. 74—77° (air-dry; corr.) or 103° (dry; corr.), and has $[\alpha]_D^{15°} + 49·9°$ (air-dry substance in water, $c = 2·5$) or $+ 56·4°$ (dry substance in water, $c = 2·5$), is neutral in reaction, fairly soluble in water or chloroform and sparingly soluble in ether (Found: loss on drying in a vacuum at 60° and finally at 90°, 9·84. $C_9H_{14}O_3,H_2O$ requires H_2O, 9·57%. Found in dried substance: C, 63·4, 63·7; H, 8·4, 8·5. $C_9H_{14}O_3$ requires C, 63·5; H, 8·3%).

No methoxyl or dioxymethylene group is present. The substance dissolves in solutions of sodium hydroxide, and the excess of alkali can be titrated back by standard hydrochloric acid with phenolphthalein as indicator. Such determinations indicated that the hydrated substance neutralised 20·7% of sodium hydroxide (Calc., 21·3%) and the dry substance, 23·5% (Calc., 23·5%). A solution in the calculated quantity of sodium hydroxide solution was concentrated, and kept after the addition of dry alcohol, when the corresponding *sodium* salt was obtained as a hygroscopic, crystalline substance (Found: loss on drying at 90—100° in a vacuum, 15·99. Calc. for $2H_2O$, 14·63%. Found in dry salt: Na, 10·64. Calc. for $C_9H_{15}O_4Na$: Na, 10·94%). The substance is therefore a *lactone* of an acid $C_9H_{16}O_4$.

On boiling the lactone with five times its weight of acetic anhydride for 1 hour, concentrating the solution under reduced pressure to half its volume, pouring into water, and extracting with ether we obtained a *monoacetyl* derivative which could not be crystallised (Found for substance dried in a vacuum at 105°: C, 62·5; H, 7·8. $C_9H_{13}O_3Ac$ requires C, 62·2; H, 7·6%). On hydrolysis with alkali and distillation of the resulting liquid, after addition of excess of sulphuric acid, 32·1% of acetic acid was obtained as determined by titration (acetic acid required for $C_9H_{13}O_3Ac$, 28·3%). The residue in the flask, on thorough extraction with chloroform, yielded 79·3% by weight of the original substance used (Calc. for $C_9H_{14}O_3$ from $C_9H_{13}O_3Ac$, 80·2%). The recovered lactone had m. p. 98—100° and $[\alpha]_D^{15°} + 55·8°$ after drying in a vacuum at 100°.

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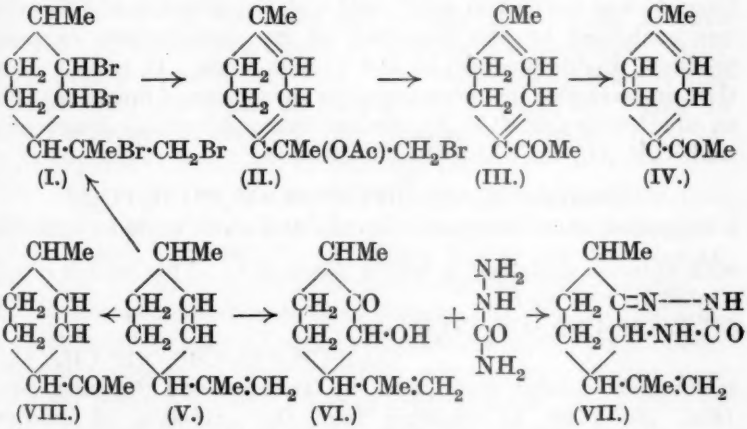
CCXIX.—*Chenopodium Oil. Part II. The Hydrocarbon Fraction.*

By THOMAS ANDERSON HENRY and HUMPHREY PAGET.

THE presence of a lævorotatory component in the hydrocarbon fraction of chenopodium oil was first recognised by Kremers (*Pharm. Rev.*, 1907, **25**, 155), and since then numerous efforts have been made to isolate and identify it. Nelson obtained, by bromination of the hydrocarbon fraction, a substance which he regarded as *l*-limonene tetrabromide (*J. Amer. Chem. Soc.*, 1920, **42**, 1204), but on repeating this work the authors found that the product so obtained was optically inactive, differed in crystalline form and physical constants from all the known terpene tetrabromides, and therefore could not be *l*-limonene tetrabromide, but must be derived from a terpene so far unknown. Up to that time only *p*-cymene and α-terpinene had been definitely recognised as present (J., 1921, **119**, 1714).

The authors now show that Nelson's tetrabromide (I) on treatment with silver acetate yields an acetoxybromide (II), which is oxidised by chromic acid to *p*-tolyl methyl ketone (IV), probably through the dihydroketone (III). These reactions are best explained



by the assumption that the tetrabromide is derived from the terpene $\Delta^{2:8(9)}$-*p*-menthadiene (V). Support for this view is obtained from the fact that the total hydrocarbon fraction on treatment with chromic acid is partly oxidised to dimethylacetonylacetone (derived from α-terpinene) and a hydroxy-ketone, $C_{10}H_{16}O_2$ (VI), the semicarbazone of which readily loses water, like other *o*-hydroxy-ketones derived from hydroaromatic substances

(compare Manasse, *Ber.*, 1897, **30**, 668), forming a base, $C_{11}H_{17}ON_3$ (VII). Further, the total hydrocarbon fraction on oxidation by permanganate yields a minute quantity of a substance, $C_9H_{14}O$, which may be tetrahydro-*p*-tolyl methyl ketone (VIII). The substances $C_{10}H_{16}O_2$ and $C_9H_{14}O$ are not obtainable by the separate oxidation of any of the known components (*p*-cymene, α-terpinene, *l*-limonene; see below) of the total hydrocarbon fraction, and it is consequently assumed that they come from the terpene* yielding the tetrabromide.

The same formula has been used already for Tschugaeff's *iso*-limonene (*J. Russ. Phys. Chem. Soc.*, 1904, **36**, 988) and Aschan's diprene (*Annalen*, 1924, **439**, 221), neither of which has been fully described, and it is possible that further work may prove all three to be identical, in which case the name *iso*limonene should have priority. It is of interest to note that all three occur along with limonene.

The removal of the readily oxidisable components (α-terpinene and terpene *A*) by partial oxidation of the total hydrocarbon fraction with chromic acid leaves a mixture of *p*-cymene and the lævorotatory component, the identity of which has been a subject of conjecture since 1907. On bromination followed by removal of the *p*-cymene, which inhibits crystallisation, *l*-limonene tetrabromide was isolated in good yield and the presence of *l*-limonene was confirmed by the formation of its characteristic oxidation products, hydroxyterpenylic and lævulic acids. It is also shown that on oxidation by permanganate in acetone, *l*-limonene yields an oily lactone acid, $C_9H_{14}O_5$, derived from a dihydroxy-dicarboxylic acid, $C_9H_{16}O_6$, for which the constitution

$$OH\cdot CHMe\cdot CH_2\cdot CH_2\cdot \overset{*}{C}H[CH(OH)\cdot CO_2H]\cdot CH_2\cdot CO_2H$$

is suggested, since it furnishes lævulic and acetic acids by oxidation with chromic acid, fission taking place at $\overset{*}{C}$. This acid is closely related to two acids,

$$CH_2Ac\cdot CH_2\cdot CHAc\cdot CH_2\cdot CO_2H \longrightarrow CO_2H\cdot CH_2\cdot CH_2\cdot CH(CO_2H)\cdot CH_2\cdot CO_2H,$$

mentioned, without description, by Tiemann and Semmler (*Ber.*, 1895, **28**, 2150) as resulting from the oxidation of limonene erythritol.

In the course of this work large quantities of the total hydrocarbon fraction of chenopodium oil have been worked up, and from the first runnings of these a few c.c. of a substance, which is probably *sym*-dimethylethylene oxide, C_4H_8O, was isolated.

* To save space, and to avoid further additions to the synonymy of terpenes, this component is referred to later as terpene *A*.

The following substances have now been identified as components of chenopodium oil.

p-Cymene.	*sym*-Dimethylethylene oxide (?).	Ascaridole.
α-Terpinene.	Butyric acid.	Ascaridole glycol.
$\Delta^{2,8(9)}$-*p*-Menthadiene.	Methyl salicylate.	Ascaridole glycol anhydride.
l-Limonene.	Salicylic acid.	

The chief interest of chenopodium oil lies in its use as an anthelmintic, and it is being employed on a large scale in anti-hookworm campaigns in various parts of the world. Drs. Smillie and Pessôa, who have been engaged in researches on hookworm disease under the auspices of the Brazilian Government and the Rockefeller Foundation in Brazil, have kindly tested pharmacologically and clinically the chief components of chenopodium oil isolated in these laboratories, and their results have been published elsewhere (*J. Pharm. Expt. Ther.*, 1924, 24, 359). They show that ascaridole, the chief component of the oil, is a remarkably efficient anthelmintic, and that none of the other constituents can be regarded as of value for this purpose.

Experimental.

When a receiver cooled in ice and salt was inserted during the separation of the hydrocarbon fraction from ascaridole by distillation at low pressure, a small amount of a colourless, volatile, pungent-smelling liquid was collected. On redistilling this, a little was obtained at 65—75°/760 mm., the greater part boiling between 120—170°, and consisting chiefly of terpenes and *p*-cymene. After drying over potassium carbonate, the lower-boiling fraction had b. p. 64—78°, $d_{15^\circ}^{15^\circ}$ 0·837, $d_{0^\circ}^{0^\circ}$ 0·8409, $[\alpha]_D^{15^\circ}$ + 0·10°, $n_D^{20^\circ}$ 1·3968 to 1·3981, *M* (vapour density) 70·2 (Found: C, 66·4; H, 12·4. C_4H_8O requires C, 66·7; H, 11·1%; *M*, 72).

The odour and the characters of this substance indicate that it might be one of the butylene oxides (possibly *sym*-dimethylethylene oxide), b. p. 56—57; $d_{0^\circ}^{0^\circ}$ 0·8344, but, as the figures given above show, the small quantity obtained was still highly impure.

The hydrocarbon fraction distilled between 170° and 185°/760 mm. but all attempts to isolate fractions of constant boiling point failed; considerable separation was, however, effected by repeated slow distillation through a 12-bulb Young dephlegmator. Four litres of the hydrocarbon fraction so treated gave the following results:

Fraction	1	2	3	4	5
B. p.	170—174°	174°	174—175°	175—175·5°	175·5—176°
Amount (g.)	20	40	150	1100	30
α (1-dcm.) ...	−14°	−15°	−16°	−17°	−17·5°
Fraction	6	7	8	9	
B. p.	176—177°	177—178°	178—180°	180—184°	
Amount (g.)	800	800	900	150	
α (1-dcm.) ...	−18°	−19°	−20°	−18·5°	

α-Terpinene nitrosite could be obtained from all these fractions, while only fractions 1 to 4 gave the tetrabromide, m. p. 117°, characteristic of terpene *A*, the best yield being obtained from fraction 1. Fraction 4 was repeatedly redistilled to furnish a little more of fractions 1 to 3, and the residue used with fractions 6, 7, and 8 for the identification of the lævorotatory component. It was shown previously (*loc. cit.*, 1717) that the α-terpinene present in these fractions could be removed by agitation with Beckmann's chromic acid mixture, leaving the lævorotatory terpene mixed with *p*-cymene, and this mixture is referred to later as fraction B. It has the following average characters: b. p. 176·5° to 177°/758 mm., $d_{23^\circ}^{23^\circ}$ 0·8545, $[\alpha]_D^{15^\circ}$ — 23·08°, $n_D^{20^\circ}$ 1·48637 [Found: C, 89·1, 88·9, 88·8; H, 10·9, 10·6, 10·65%, which corresponds with a mixture of terpenes $C_{10}H_{16}$ (C, 88·2; H, 11·8) and *p*-cymene $C_{10}H_{14}$ (C, 89·6; H, 10·4) in proportion 40 : 60, and 63% of *p*-cymene can be isolated from it by oxidation with permanganate in acetone (see below)]. It yields no terpinene nitrosite, nor any of the oxidation products of α-terpinene, and no terpene *A* tetrabromide could be obtained from it.

Examination of Fraction B.

Bromination.—On bromination by the method already described (*loc. cit.*, p. 1717) a yellow, viscous oil was obtained which, even after standing for several months below 0°, deposited no crystals and gradually changed to a nearly solid tar. If, however, the freshly-brominated product, freed from chloroform and hydrogen bromide by aspiration, was quickly distilled until the bulk of the *p*-cymene was removed at about 105°/10 mm., the residual brown oil, on standing, became filled with leafy crystals, m. p. 104° after recrystallisation from alcohol. A mixture with an equal quantity of *d*-limonene tetrabromide melted at 124° and showed no depression of melting point on further admixture with dipentene tetrabromide. A mixture with the tetrabromide of terpene *A* (m. p. 117°) melted at 90—92°. The substance is therefore *l*-limonene tetrabromide (Found: Br, 69·9; $[\alpha]_D^{16^\circ}$ — 66·12°. *l*-Limonene tetrabromide, $C_{10}H_{16}Br_4$, requires Br, 70·2% and has $[\alpha]_D^{9^\circ}$ — 73·45°).

Oxidation by Permanganate in Acetone.—Fraction B (700 c.c.) mixed with acetone was treated with powdered potassium permanganate (1200 g.) in quantities of 10 g. at a time. The acetone was then distilled off and the residue steam-distilled, yielding 436 c.c. of *p*-cymene (62·3% of the mixture used) having α — 0·7°. The residual alkaline liquor, combined with the washings of the precipitated manganese dioxide, was concentrated to low bulk (compare *loc. cit.*, p. 1719), shaken with ether and ethyl acetate

to remove a small amount of neutral matter, from which traces of the carbonyl compound $C_9H_{14}O$ were isolated (p. 1658), then acidified and again extracted with ether (i), and ethyl acetate (ii). After removal of acetic acid by heating under reduced pressure, these extracts amounted to (i) 61·3 g. and (ii) 15·6 g. and consisted of oily acids, which could not be induced to crystallise either as such or in the form of derivatives. They were therefore converted into ethyl esters, and these distilled under reduced pressure, giving fraction (a), b. p. 117—170°/11 mm., $[\alpha]_D^{20°} - 4·8°$; fraction (b), b. p. 170—215°/11 mm., $[\alpha]_D^{20°} - 4·8°$, which from the long range of boiling point were obviously mixtures.

After many attempts to isolate a pure acid from these esters it was found that by hydrolysing them with sodium hydroxide in alcohol, a sodium salt, insoluble in alcohol, was produced, which though hygroscopic could be obtained in a granular condition by filtering rapidly from the excess of alcoholic soda, washing thoroughly with 96% alcohol, and drying in a vacuous desiccator. More of this sodium salt was secured by distilling the solvent from the mother-liquors and boiling the residue with dry alcohol. Finally, the viscous residual mixture of soluble sodium salts was dissolved in water, shaken with ether to remove a small amount of neutral tar that had formed, then acidified, and the liberated acid recovered by extraction with ether. This solvent having been distilled off, the acid was boiled with baryta, the excess of the latter removed by carbon dioxide, the filtrate taken to dryness in a vacuum, and the residue boiled with alcohol, which caused the separation of an insoluble barium salt, a little more of which was obtained by repeating the process. Finally, there was left a comparatively small amount of a mixture of barium salts soluble in alcohol, from which a little more material could be separated by precipitation as the thorium salt, but this method was not pursued further. The insoluble sodium and barium salts, isolated as described above, were purified as far as possible by repeated boiling with 96% alcohol, and then gave the following results on analysis, which showed them to be salts of the same acid. *Sodium* salt. Found: Na, 17·0%. *Barium* salt, Found: Ba, 39·1%. Calc. for $C_9H_{14}O_6Na_2$, Na, 17·4%; calc. for $C_9H_{14}O_6Ba$, Ba, 38·6%. The free acid, regenerated from either the sodium or barium salt, boiled at about 210°/34 mm. and formed a colourless, viscid oil (Found: C, 54·0, 53·9; H, 6·4, 6·8. $C_9H_{14}O_5$ requires C, 53·5; H, 6·9%).

On direct titration with *N*-soda solution no definite end-point could be obtained, but when the acid was boiled with excess of *N*-soda for at least 30 minutes and the excess of alkali titrated

back with *N*-acid satisfactory end-points were reached and the amount of soda used was equivalent on the average to sodium (Na) 22·19%. For conversion of $C_9H_{14}O_5$ into $C_9H_{14}O_6Na_2$ the amount of sodium (Na) required is 22·7%.

The silver salt of the acid is relatively stable at atmospheric temperatures even on exposure to light; it dissolves in boiling water and if the solution is filtered rapidly from the small amount of reduced silver formed, re-deposits the salt on cooling as a colourless granular powder, which, however, cannot be dried for analysis without the application of heat, which leads to reduction; and the results are always from 2 to 4% high in silver. Small amounts of the barium salt have been obtained in crystalline form by the cautious addition of alcohol to a 25% solution of the salt in water, but the crystals are very deliquescent, and it was not found practicable to secure enough crystallised barium salt for examination in this way.

The acid gave no derivative with semicarbazide, hydroxylamine, or phenylhydrazine.

To a solution of 2·6 g. of the sodium salt in 30 c.c. of water 30 c.c. of Beckmann's chromic acid mixture were added and the mixture was left standing with occasional agitation for 4 days. It was then thoroughly extracted with ether, which removed 1·52 g. of oily acids, smelling strongly of acetic acid. This residue was left in a vacuum over caustic potash until the bulk of the acetic acid was removed, and then treated with solution of semicarbazide in alcohol, when in the course of a few hours it deposited a copious crop of crystals of a semicarbazone, m. p. 182°; after recrystallisation from alcohol, this rose to 194° (corr.) and showed no change on further crystallisation and no depression when mixed with lævulic acid semicarbazone. The oxidation products of the $C_9H_{14}O_5$ acid are therefore lævulic and acetic acids, and in view of this and the results recorded above the authors regard this acid as a lactone of the acid $OH{\cdot}CHMe{\cdot}CH_2{\cdot}CH_2{\cdot}CH[CH(OH){\cdot}CO_2H]{\cdot}CH_2{\cdot}CO_2H$ (p. 1650).

The acids regenerated from the barium salts soluble in alcohol referred to above also yield lævulic and acetic acids on oxidation with chromic acid and therefore probably still contain some of the $C_9H_{14}O_5$ lactone acid, which seems to be the principal product of the oxidation of limonene by permanganate in acetone solution.

Oxidation by Permanganate in Water.—Fraction B (100 c.c.) was added in four portions to 1 litre of water containing 94 g. of potassium permanganate, and shaken occasionally till decolorised. The mixture was then steam-distilled to remove unchanged hydrocarbon, and the residual liquor in the distillation flask, with the washings from the precipitated manganese dioxide, thoroughly

extracted with ether, yielding a little cuminaldehyde (derived from *p*-cymene), which was identified by a mixed melting point determination of the semicarbazone (m. p. 210°). The liquor was then concentrated to low bulk, made acid, and shaken with (i) ether and (ii) ethyl acetate. The ethereal extract after removal of the solvent was distilled under reduced pressure, and yielded two fractions, the first a thick oil and the second crystalline, m. p. 159—160°, and consisting of *iso*propenylbenzoic acid, formed by distillation of hydroxy*iso*propylbenzoic acid, which is known as an oxidation product of *p*-cymene under these conditions (Found: C, 73·6; H, 6·4. Calc. for $C_{10}H_{10}O_2$: C, 74·1; H, 6·2%. Found in silver salt: Ag, 40·9. Calc. for $C_{10}H_9O_2Ag$: Ag, 40·15%). The oily fraction gave a semicarbazone, which after recrystallisation melted constantly at 194° and showed no depression of melting point when mixed with lævulic acid semicarbazone (Found: C, 41·9; H, 6·7. Calc. for $C_6H_{11}O_3N_3$: C, 41·6; H, 6·3%). The ethyl acetate extract, on removal of the solvent, deposited a crystalline acid, m. p. 195° (Found: C, 50·2; H, 6·4. $C_8H_{12}O_5$ requires C, 50·85; H, 6·4%). The substance remained unchanged in m. p. after recrystallisation from boiling alcohol and produced no depression when mixed with hydroxyterpenylic acid, $C_8H_{12}O_5$, already known as an oxidation product of *d*-limonene (Godlewski, *J. Russ. Chem. Soc.*, 1899, **31**, 211).

As lævulic acid has not been previously mentioned as formed in the oxidation of limonene by permanganate in water, commercial limonene was oxidised as described above, and yielded hydroxyterpenylic and lævulic acids, but no cuminaldehyde or *iso*propenylbenzoic acid.

From the foregoing results it is clear that fraction B of the chenopodium oil hydrocarbons contains, in addition to *p*-cymene, *l*-limonene.

Nature of Terpene A.

As already stated, it has not been possible to isolate this terpene, or to obtain mixtures containing more than 10 to 12% of it as indicated by the amount of tetrabromide obtainable. For evidence of its constitution reliance has therefore had to be placed on (i) reactions of the only crystalline derivative, the tetrabromide, and (ii) the formation of certain substances when mixtures containing it are oxidised.

Oxidation of the Total Hydrocarbon Fraction by Chromic Acid.—The total hydrocarbon fraction of chenopodium oil was oxidised as already described (*loc. cit.*, p. 1717). After separation by steam distillation of the unattacked hydrocarbons (2150 c.c. from 2500 c.c.) there remained in the distillation flask 70 g. (about 1·5%) of a thick

oil, which, after drying, was distilled under reduced pressure, yielding an oil, b. p. 138—154°/19 mm., and a hard, pitch-like residue, which decomposed on further heating. The oil, after standing in solution in ether over potassium carbonate, was redistilled in two fractions, b. p. 110—120°/15 mm. and 120—136°/15 mm. Both were pale yellow, viscous oils having a faint carvone-like odour; they yielded no solid derivatives with phenylcarbimide or *p*-nitrobenzoyl chloride, but on addition of semicarbazide in aqueous acetic acid solution were converted in the course of 3 days into semi-solid masses, which, when rubbed with alcohol, became crystalline, m. p. 140° (air-dry) and 194° when completely dried at 100°; after recrystallisation from boiling alcohol, they melted at 157° (air-dry) or 204° (dried at 120° in a vacuum), and these melting points were unchanged after a further crystallisation from alcohol. The acetic acid of crystallisation (see below) persists when the air-dry substance is crystallised from boiling alcohol, but if the dried substance is recrystallised from alcohol or boiling water the product obtained melts at 204° and is anhydrous. From all solvents the substance forms rosettes of transparent prisms [Found: loss on drying at 120° in a vacuum, 21·2%. $C_{11}H_{19}O_2N_3,C_2H_4O_2$ requires loss (acetic acid), 21·05%. Found in dried material: C, 58·6, 58·7; H, 8·6, 8·4; N, 19·2. $C_{11}H_{19}O_2N_3$ requires C, 58·6; H, 8·5; N, 18·6%]. The substance is therefore a *semicarbazone* of a product, $C_{10}H_{16}O_2$, probably a *keto-alcohol*. When the semicarbazone is formed in presence of alcohol and acetic acid, or when it is repeatedly boiled with water, there is formed a *base* which has only been isolated as the *acetate*, minute rosettes of needles, m. p. 206°, from water by slow evaporation, and the *picrate*, brilliant yellow needles, m. p. 158°, from acetone or acetone and benzene. This differs from the semicarbazone by the elements of a molecule of water [Found (i) in acetate: C, 57·5, 58·2; H, 8·3, 8·1. $C_{11}H_{17}ON_3,C_2H_4O_2$ requires C, 58·05; H, 7·8%. Found (ii) in picrate: N, 18·6. $C_{11}H_{17}ON_3,C_6H_2(NO_2)_3{\cdot}OH$ requires N, 19·3%].

It is clear from this that the semicarbazone readily undergoes internal condensation, losing a molecule of water, and on this account it is regarded as having the constitution represented by formula (VI), and the base $C_{11}H_{17}ON_3$ formed from it as having formula (VII).

Only part of the oil reacts with semicarbazide solution and after the whole of the semicarbazone has been separated the mother-liquor on dilution with water yields a thick oil, which can be extracted with ether. This could not be induced to crystallise, nor could it be distilled without some decomposition. It appears,

however, to be a derivative of α-terpinene, since on oxidation with aqueous permanganate it gave a good yield of the mixed *anti*- and *para*-forms of αδ-dihydroxy-α-methyl-δ-*iso*propyladipic acid, m. p. 189°, and showed no depression of melting point on addition of a recrystallised mixture in equal parts of these two forms of this acid (J., 1923, **123**, 1878).

In this oxidation by Beckmann's mixture, α-terpinene is converted into dimethylacetonylacetone, the yield being about 3% of the total hydrocarbon fraction taken. The substance was identified by conversion into the semicarbazide derivative, which melted at 201° and showed no depression of melting point when mixed with the semicarbazide derivative prepared from synthetic dimethylacetonylacetone (Found: C, 59·2; H, 8·9; N, 23·05. Calc. for $C_9H_{15}ON_3$: C, 59·7; H, 8·3; N, 23·2%). Some *p*-tolyl methyl ketone was also formed in the oxidation, and was identified by means of its semicarbazone (Found: C, 62·1; H, 6·6. Calc., C, 62·8; H, 6·8%), m. p. 210°, which showed no depression when the substance was mixed with *p*-tolyl methyl ketone semicarbazone. α-Terpinene, *d*-limonene, and *p*-cymene have all been treated separately with Beckmann's mixture, and their oxidation products are being examined, but none of them yields the substance $C_{10}H_{16}O_2$ described above, and it seems safe to assume that this is derived from terpene *A*.

Oxidation of the Total Hydrocarbon Fraction by Permanganate in Acetone.—When the total hydrocarbon fraction is oxidised by permanganate in acetone, the principal products are a mixture of the *para*- and *anti*-forms of αδ-dihydroxy-α-methyl-δ-*iso*propyladipic acids already described by the authors (J., 1923, **123**, 1878) and dimethylacetonylacetone, resulting from the further oxidation of these acids derived from α-terpinene, *p*-tolyl methyl ketone, and a little cuminic acid, both arising from *p*-cymene, and a mixture of optically active oily acids identical with those, described above (p. 1653), derived from *l*-limonene. The only other product was obtained by extracting the concentrated neutral aqueous liquors with ether, which removed a viscous, brown oil too small in amount to permit of direct purification. From this a crystalline semicarbazone was obtained, which on recrystallisation from boiling alcohol formed colourless needles, m. p. 204° (corr.), which became yellow on exposure to light (Found: C, 61·3, 61·5; H, 8·7, 8·15; N, 21·3. $C_{10}H_{17}ON_3$ requires C, 61·5; H, 8·7; N, 21·5%). On hydrolysis, the semicarbazone furnishes an oil smelling like a mixture of menthone and cuminaldehyde, and from this oil the semicarbazone cannot be regenerated. This semicarbazone is optically inactive, and, if it comes from terpene *A*, should be

that of Δ^2-tetrahydro-*p*-tolyl methyl ketone, $C_9H_{14}O$ (VIII), but as the yield of semicarbazone obtained only amounts to 0·24% of the total hydrocarbon fraction used, it has not been possible to accumulate enough for examination in detail.

Tetrabromide of Terpene A.—The preparation and isolation of the tetrabromide has been described already (*loc. cit.*, p. 1717). Of numerous attempts to use this tetrabromide as a means of gaining information regarding the constitution of terpene *A*, only the following have given useful results. 12·5 G. of the tetrabromide were added to a solution of 1·9 g. of sodium in methyl alcohol, and the mixture, after boiling for 7 hours, was steam-distilled, when 4·4 g. of a heavy, colourless oil were obtained, b. p. 115—120°/18 mm., containing 30·2% of bromine ($C_{10}H_{14}Br{\cdot}OMe$ requires Br, 32·6%). This appeared to be a monobromomethyl ether corresponding to the monobromomethyl ether which Wallach obtained from limonene tetrabromide (*Annalen*, 1894, **281**, 127). The removal of the fourth bromine atom by the further use of sodium converted the monobromomethyl ether almost wholly into *p*-cymene. Unlike Wallach's product, it did not after reduction yield a menthenone by oxidation with either chromic acid or permanganate. It was only slowly attacked by either agent, and the products in both cases were *p*-tolyl methyl ketone with a little *p*-toluic acid. In further experiments, silver acetate was used: 5·3 g. of the tetrabromide were shaken with 5·8 g. of silver acetate in 10 c.c. of acetic acid during 8 hours, then made alkaline with sodium carbonate, and shaken with ether, which removed a yellow, viscous oil (3·1 g.). This on solution in light petroleum (b. p. 40—60°) deposited some insoluble tar, and the oil thus purified, after drying over potassium carbonate and removal of the petroleum by distillation and exposure in a vacuum until of constant weight, gave the following results: C, 52·8; H, 6·1; Br, 29·2 ($C_{10}H_{14}Br{\cdot}O{\cdot}CO{\cdot}CH_3$ requires C, 52·6; H, 6·2; Br, 29·3%). The substance is therefore a *bromoacetoxydihydro*-p-*cymene* (II) and this was confirmed by hydrolysing a weighed quantity (0·2175 g.) of the substance in the cold with a known amount of potassium hydroxide in alcohol (30·6 c.c. of *N*/10-KHO), the mixture being allowed to stand for a week, after which the excess of alkali (16·42 c.c. of *N*/10-KHO) was determined by titration with standard nitric acid. The amount of alkali used (14·2 c.c of *N*/10-KHO), after correction for a small amount of bromide (equal to 0·0478 g. Br) formed, was 21·1%, whilst that required for the removal of one acetyl group from $C_{10}H_{14}Br{\cdot}O{\cdot}CO{\cdot}CH_3$ is 20·5%.

Seven g. of the bromoacetoxy-compound were agitated with 30 c.c. of water to form an emulsion; to this 130 c.c. of Beckmann's

chromic acid mixture were added in three portions at intervals of 1 hour, and the whole was shaken for 8 hours. This was extracted with (1) light petroleum, b. p. 40—60°, and (2) ether, and the extracts were dried over anhydrous sodium sulphate. The petroleum extract (1) left an oily residue (2·9 g.) which was pungent, and had an odour of *p*-tolyl methyl ketone; on treatment with semicarbazide it yielded a semicarbazone which after crystallising twice from boiling alcohol formed colourless, opaque prisms melting constantly at 210° and showing a slight rise in melting point to 211° when mixed with an equal quantity of *p*-tolyl methyl ketone semicarbazone prepared from synthetic material. The mother-liquor from the preparation of the semicarbazone was made alkaline with sodium carbonate and shaken with light petroleum, when it yielded 1·7 g. of an oil containing bromine and apparently consisting largely of unchanged material. The ether extract (2) yielded on re-extraction with sodium carbonate solution and acidification of this (*a*) terephthalic acid, colourless crystals, subliming without melting above 280°, and (*b*) *p*-toluic acid, m. p. 177°, showing no depression when mixed with a pure specimen of *p*-toluic acid.

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WELLCOME CHEMICAL RESEARCH LABORATORIES,
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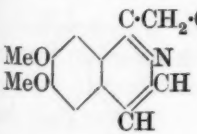
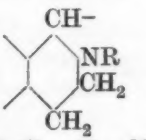
CCXX.—iso*Quinoline Derivatives. Part IX. Preparation and Reduction of* iso*Quinoline and its Derivatives.*

By ROBERT FORSYTH, CHARLES IGNATIUS KELLY, and FRANK LEE PYMAN.

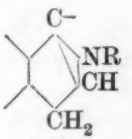
THE reduction of papaverine (I) and *N*-methylpapaverinium salts by means of tin and hydrochloric acid yields not only the expected tetrahydro-derivatives (II), but also, as by-products, the 2 : 4-dihydro-derivatives, pavine and *N*-methylpavine, containing the unique dicyclic system (III) (Pyman, J., 1915, **107**, 176, where earlier references are given). The present inquiry had the object



(I.)



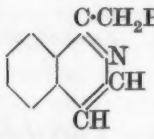
(II.) (R = H or Me)



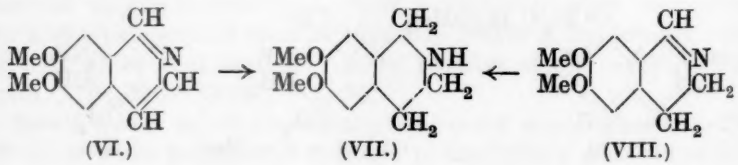
(III.)

of determining whether the formation of by-products of this type on the reduction of *iso*quinoline, by means of tin and hydrochloric acid, is a general property or not, and necessitated a quantitative study of the reduction of pure materials, for the quantities of these by-products to be expected were only small. Thus, the yields of pavine isolated by different investigators range from 8 to about 25% (Pope and Gibson, J., 1910, **97**, 2207), whilst the yield of *N*-methylpavine was 3% of the theoretical.

The reduction of *iso*quinoline itself was first examined, for uncharacterised by-products of its reduction to tetrahydro*iso*quinoline have been noticed by former investigators, and it was uncertain whether these were of the pavine type or due to impurities in the initial material. Experiments showed that pure *iso*quinoline can be reduced to tetrahydro*iso*quinoline in nearly theoretical (96%) yield. The effect of a 1-benzyl group was next studied, and here 1-benzyl*iso*quinoline methiodide gave 1-benzyl-2-methyltetrahydro*iso*quinoline in a yield of 85% of the theoretical, unaccompanied by any other organic base, the deficit being due to partial decomposition of the material with the formation of ammonia. Similarly, the only product isolated after reduction of 1-benzyl-*iso*quinoline (IV) was 1-*benzyl*-1 : 2 : 3 : 4-*tetrahydro*iso*quinoline* (V). The constitution of this substance was proved by its conversion into 1-benzyl-2-methyltetrahydro*iso*quinoline on methylation.

(IV.)  (V.)

The effect of methoxy-substituents in the *iso*quinoline nucleus was next examined, and here also a negative result was obtained, for 6 : 7-dimethoxy*iso*quinoline (VI) gave 6 : 7-*dimethoxy*-1 : 2 : 3 : 4-*tetrahydro*iso*quinoline* (VII) in a yield of 94% of the theoretical. The identity of the product was established by comparison with the product of reduction of 6 : 7-dimethoxy-3 : 4-dihydro*iso*quinoline (VIII) (Pyman, J., 1909, **95**, 1610). Similarly, the reduction of 6 : 7-*dimethoxy*iso*quinoline methiodide* gave as the sole isolable product 6 : 7-dimethoxy-2-methyltetrahydro*iso*quinoline (Pyman, J., 1909, **95**, 1266).



(VI.) (VII.) (VIII.)

It has thus been shown that neither a 1-benzyl nor 6 : 7-dimethoxy-groups suffice to induce formation of compounds of the pavine type on the reduction of derivatives of *iso*quinoline, and the further investigation of this problem, which is contemplated, will necessitate the preparation and reduction of 1-benzyl-6 : 7-dimethoxy*iso*-quinoline and possibly also of 1-veratryl*iso*quinoline.

Of the *iso*quinoline derivatives required for this work, a part of the *iso*quinoline itself was isolated from coal tar by fractionation and crystallisation of the acid sulphate as described below, the yield being better than that obtained by Harris and Pope (J., 1922, **121**, 1029), using another method. Several methods for the preparation of 1-benzyl*iso*quinoline were examined, and of these the only satisfactory one was that of Decker and Pschorr (*Ber.*, 1904, **37**, 3397) by the action of benzyl magnesium chloride on *N*-methyl*iso*quinolone and distillation of the 1-benzyl*iso*quinoline methiodide produced. The oxidation of 1-benzyl-3 : 4-dihydro-*iso*quinoline (Pictet and Kay, *Ber.*, 1909, **42**, 1973) gave only 3% of 1-benzyl*iso*quinoline, and the dehydration of α-hydroxy-β-phenyl-acetylamino-α-phenylethane (A) by phosphorus pentoxide gave only 4% of 1-benzyl*iso*quinoline. This last result is in accord with the work of Robinson (J., 1909, **95**, 2167), who obtained only a trace of a picrate, suspected of being 1-benzyl*iso*quinoline picrate, in this way, and is at variance with the results of Pictet and Gams (*Ber.*, 1910, **43**, 2386), who obtained a 40% yield. The latter authors, like Robinson, prepared the carbinol (A) by the reduction of ω-phenylacetylaminoacetophenone, but found it to melt at 123°, whereas Robinson found the m. p. 99°. Here, again, our results confirm those of Robinson, the carbinol (A) proving to melt at 99° whether prepared by Robinson's method or by the action of phenyl-acetyl chloride upon β-hydroxy-β-phenylethylamine.

The preparation of 6 : 7-dimethoxy*iso*quinoline was effected essentially by the method of Rügheimer and Schön (*Ber.*, 1909, 42, 2374), that is, by the action of sulphuric and arsenic acids upon veratrylaminoacetal, but the technique has been improved. Veratrylaminoacetal was prepared by the reduction of *veratrylidene-aminoacetal*, a more convenient method than the action of chloro-acetal upon veratrylamine, the method of the previous authors (*Ber.*, 1908, **41**, 17).

EXPERIMENTAL.

Preparation of iso*Quinoline.*—Three gallons of "crude pyridine bases" (corresponding to 6 tons of coal tar) were dehydrated by shaking three times with aqueous sodium hydroxide (80° Tw.), and the product (10·85 litres) was distilled up to 170° and then fractionated through a 12-pear column. The various fractions,

b. p. 200—280°, were fractionated similarly twice more, when 2·3 litres (2470 g.) of "heavy quinoline bases," b. p. 230—255°, were obtained. This fraction was converted into acid sulphate, and crystallised fractionally from alcohol, when 185 g. of pure *iso*quinoline hydrogen sulphate, m. p. 207·5° (corr.), were obtained. This gave 102 g. of the base, b. p. 242° (corr.) over a range of 0·5°; m. p. 24° (corr.). The yield of *iso*quinoline from the "heavy quinoline bases" is thus about 4%, whereas Harris and Pope (who refer to previous work on the subject, J., 1922, **121**, 1029) obtained only 1·5% by a more laborious method.

Reduction of iso*Quinoline.*—*iso*Quinoline (6·45 g.), alcohol (68 c.c.), hydrochloric acid (100 c.c. conc.), and granulated tin (42 g.) were heated on the water-bath under reflux for 12 hours. After cooling, the separated tin salts were collected (mother-liquor M) and deprived of tin by means of hydrogen sulphide, when, on evaporation, crude tetrahydro*iso*quinoline hydrochloride (8·0 g.; m. p. 195°) was obtained. It was mixed with aqueous sodium hydroxide and distilled into hydrochloric acid, and the distillate gave, on evaporation, pure tetrahydro*iso*quinoline hydrochloride (7·83 g.; m. p. 196—197°. Hoogewerf and van Dorp, *Rec. trav. chim.*, 1885, **4**, 125, give m. p. 195—197°). The residue from the steam-distillation was extracted with chloroform, which removed a base giving a crystalline hydrochloride, the total residue as hydrochloride, m. p. 280—290°, amounting to only 0·05 g. The mother-liquor M gave, after removal of tin, crude tetrahydro*iso*quinoline hydrochloride (0·3 g.; m. p. 190°; m. p. of mixture with the pure salt, 192°). The total yield of tetrahydro*iso*quinoline is thus 96·35% of the theoretical. To establish its purity, 8·0 g. were mixed with carbon disulphide in dry ether, and the precipitated tetrahydro*iso*quinoline tetrahydro*iso*quinolyldithiocarbamate (Bamberger and Dieckmann, *Ber.*, 1893, **26**, 1208) was decomposed with hydrochloric acid, when 7·86 g. of tetrahydro*iso*quinoline hydrochloride of unchanged m. p. were recovered.

1-*Benzyl*iso*quinoline.*—*A.* After Decker and Pschorr (*Ber.*, 1904, **37**, 3397). Five g. of 1-benzyl*iso*quinoline methiodide (from *N*-methyl*iso*quinolone and benzyl magnesium chloride; yield 36% of pure salt, m. p. 248° [corr.]) were heated under 20—30 mm. until all methyl iodide was removed; the residue then distilled at 222° (corr.)/18 mm. Decker and Pschorr give 211—213°/11 mm. The distillate, which crystallised and melted at 55—56° (corr.), was converted into the hydrochloride, and more of this salt was recovered from the distillation residue (yield 3·5 g. = 86%). This salt crystallises from water in colourless, elongated prisms, which contain $2H_2O$ and melt below 100°, but after drying first in a vacuum

and then at 100°, the substance melts at 185—187° (corr.). Decker and Pschorr give m. p. 171—172°; Pictet and Gams, 175° (Found: H_2O, 12·0. Calc. for $2H_2O$, 12·4%. Found, in dried salt: Cl, 13·9. Calc., Cl, 13·9%). The picrate melted at 184° (corr.). Decker and Pschorr give 184—185° (corr.).

B. After Pictet and Kay (*Ber.*, 1909, **42**, 1973). To 1-benzyl-3:4-dihydro*iso*quinoline (2 g.; b. p. 196—197°/12 mm.) in glacial acetic acid (100 c.c.) at 100°, potassium permanganate (1 g.) in water (200 c.c.) was added with shaking in 1½ hours, and the mixture was heated for another hour. After basifying, ether removed an oil (0·8 g.) which was converted into the picrate and crystallised fractionally from alcohol, when 0·11 g. of the nearly pure salt was obtained (yield 3%; m. p. 181—182° [corr.]; not depressed after mixture with an authentic specimen). Numerous attempts to improve upon this yield by varying the conditions were unsuccessful. Pictet and Kay do not state their yield, but indicate that it was poor.

C. After Robinson (J., 1909, **95**, 2167) and Pictet and Gams (*Ber.*, 1910, **43**, 2386). ω-Phenylacetylaminoacetophenone (from phenylacetyl chloride, ω-aminoacetophenone hydrochloride, and sodium hydroxide; yield 50%; m. p. 103°) was reduced by Robinson's method and gave α-hydroxy-β-phenylacetylamino-α-phenylethane (yield 73%; m. p. 99° as stated by Robinson). On attempting the reduction under the conditions employed by Pictet and Gams, a poor yield of a crude product, m. p. 73°, was obtained. α-Hydroxy-β-phenylacetylamino-α-phenylethane was also prepared by mixing 2 g. of β-hydroxy-β-phenylethylamine carbonate (Wolfheim, *Ber.*, 1914, **47**, 1440) with phenylacetyl chloride (2·5 g.) and 20% aqueous sodium hydroxide (15 c.c.), and after purification melted at 99°, alone or mixed with the substance made by Robinson's method.

α-Hydroxy-β-phenylacetylamino-α-phenylethane (40 g.; m. p. 99°) in xylene (200 c.c.) was dehydrated by phosphorus pentoxide (200 g.), and the basic products were collected as described by Pictet and Gams, and converted into the hydrochloride, when 1-benzyl*iso*quinoline hydrochloride (1·8 g.; m. p. [dry] 185°; yield 3·9%) was obtained. A specimen of the picrate prepared from this salt had m. p. 184° (corr.), alone or mixed with an authentic specimen.

Reduction of 1-*Benzyliso*quinoline.—1-Benzyl*iso*quinoline hydrochloride (4·0 g.; air-dried), alcohol (20 c.c.), concentrated hydrochloric acid (20 + 10 c.c.) * and tin-foil (10 + 2·5 g.) were digested

* In this and the following reductions additional quantities of hydrochloric acid and tin were added after some hours.

for 21 hours on the water-bath. Water was added, tin removed, and the solution concentrated and mixed with sodium iodide, when pure 1-benzyl-1 : 2 : 3 : 4-tetrahydro*iso*quinoline hydriodide (3·75 g.; anhydrous, m. p. 167—168°) separated. The filtrate was mixed with sodium hydroxide and extracted with ether, 0·2 g. of brown oil being obtained. This was not wholly basic, but gave a turbid solution with hydrochloric acid. After filtration through charcoal and addition of sodium iodide, 0·22 g. of the above iodide, m. p. (crude) 145—155° (not depressed by mixture with the pure salt), was deposited, which after crystallisation from water gave 0·15 g., m. p. 162—165°. The total yield is thus 81% of the theoretical.

1-*Benzyl*-1 : 2 : 3 : 4-*tetrahydro*isoquinoline *hydriodide*, colourless well-formed prisms from water, has m. p. (substance dried at 100°) 167—168·5° (corr.). It is sparingly soluble in cold water (Found: loss at 100°, 5·0. $C_{16}H_{17}N,HI,H_2O$ requires H_2O, 4·9%. Found, in dried salt: C, 54·8; H, 5·1; I, 36·3. $C_{16}H_{17}N,HI$ requires C, 54·7; H, 5·1; I, 36·2%). The *base* (V) was a colourless, viscous oil, which did not crystallise after keeping for 2 days over sulphuric acid in a vacuum. The *picrate* crystallised from alcohol in deep yellow, prismatic needles, m. p. 166—167° (corr.) after drying at 100°.

Methylation.—1-Benzyltetrahydro*iso*quinoline and methyl iodide were heated for a few minutes under reflux, and after removal of uncombined methyl iodide a gummy product remained, doubtless a mixture of the hydriodides of the secondary and tertiary bases with the methiodide of the latter. The bases regenerated from this by means of sodium hydroxide and ether were crystallised fractionally as picrates, when 1-benzyl-2-methyltetrahydro*iso*quinoline picrate separated first. It had m. p. 165—166° (corr.), alone or mixed with a specimen prepared by the reduction of 1-benzyl*iso*quinoline methiodide, and the hydriodides from the two sources also proved to be identical.

Reduction of 1-*Benzylisoquinoline Methiodide.*—The pure methiodide (10 g.; m. p. 248° [corr.]), alcohol (40 c.c.), hydrochloric acid (40 + 20 c.c. conc.), and tin-foil (20 + 5 g.) were heated on a water-bath under reflux for 24 hours. After distilling the alcohol, water was added, when the bulk of the organic tin salts were deposited (mother-liquor L). The gummy deposit was dissolved in water, and deprived of tin by means of hydrogen sulphide. The filtrate was evaporated under diminished pressure to remove excess of hydrochloric acid, and the residue was dissolved in water and mixed with sodium iodide, when pure 1-benzyl-2-methyl-1 : 2 : 3 : 4-tetrahydro*iso*quinoline hydriodide (8·33 g.) was deposited. Before

and after crystallisation from alcohol, it melted at 174—175° (corr.), separating from alcohol in prismatic columns as stated by Freund and Bode (*Ber.*, 1909, **42**, 1746), who give m. p. 175—180°. The picrate crystallised from alcohol in rhombic tablets, m. p. 165—166° (corr.), as stated by these authors. The mother-liquor L was deprived of tin, mixed with the filtrate from the above hydriodide, basified with sodium hydroxide, and extracted with ether, which removed an oily base (0·35 g.). This was converted into the hydriodide (0·4 g.; m. p. 166—170°) and crystallised from alcohol, when 0·25 g. of the pure salt was obtained. The total yield of the pure salt is thus 86% of the theoretical. The liquor from which the base was extracted contained ammonia. A similar result was obtained on repetition of this experiment, an 84% yield of the pure hydriodide being obtained.

6 : 7-*Dimethoxy*isoquinoline.—Veratraldehyde (52·4 g.) and aminoacetal (42 g.) were heated for several hours on the water-bath, until the water, which soon separated, had evaporated. The crude product, obtained in theoretical yield, had m. p. 53—58°, and after crystallisation from ether gave *veratrylideneaminoacetal* in nearly colourless, very pale yellow, well-formed plates, m p. 61—62° (corr.) (Found: C, 64·1; H, 8·3. $C_{15}H_{23}O_4N$ requires C, 64·0; H, 8·2%).

Crude veratrylideneaminoacetal (50 g.) in absolute alcohol * (0·5 litre) was reduced by the gradual addition of sodium (50 g.) and more alcohol. After water had been added, ether collected nearly pure veratrylaminoacetal, which, after removal of solvents at 100°/15 mm., amounted to 45 g. and was suitable for use in the next operation without distillation.

Veratrylaminoacetal has b. p. 208° (corr.)/15 mm. (Found: C, 63·4; H, 8·8. $C_{15}H_{25}O_4N$ requires C, 63·6; H, 8·8%). Rügheimer and Schön (*Ber.*, 1909, **42**, 2374), who did not analyse the compound, give b. p. 197°/11 mm.

Arsenic pentoxide (5 g.) was dissolved in warm water (1 c.c.), concentrated sulphuric acid (10 c.c.) added, and the whole cooled in a freezing mixture. Crude veratrylaminoacetal (5 g.) was run in a few drops at a time with thorough rubbing to dissolve the viscous product. A homogeneous solution was obtained in about ¼ hour, and was kept for 1 hour at the ordinary temperature, and then heated for 1 hour at 100°. The products from 10 such experiments were diluted with water (100 c.c.) and mixed with sufficient 20% aqueous sodium hydroxide to neutralise the bulk of the acid. After cooling, an amorphous precipitate was removed by filtration,

* Fusel oil (at 130°) cannot be substituted for absolute alcohol in this case.

and the liquor basified with sodium hydroxide and extracted with chloroform. (Distressing emulsions are obtained if the removal of the amorphous precipitate is omitted.) The chloroform residue was mixed with hydrochloric acid, the solution evaporated to dryness, and the residual hydrochloride crystallised several times from alcohol. From the final mother-liquors, the base was regenerated by sodium hydroxide, and extracted with chloroform. The chloroform residue was extracted twice with hot ether, and the extract converted into hydrochloride and crystallised from alcohol. In this way, veratrylaminoacetal (50 g.) gave 8·5 g. of pure 6 : 7-dimethoxy*iso*quinoline hydrochloride (dried at 100°), that is 21% of the theoretical. Rügheimer and Schön describe the yield as "satisfactory." This salt crystallises from alcohol in nearly colourless needles, containing $3H_2O$, which are lost at 100°; when anhydrous, it melts and effervesces at 221° (corr.). Rügheimer and Schön give 208—210° (decomp.). The base separated from ether in large prisms, m. p. 93° (corr.); Rügheimer and Schön give 93—94°.

6 : 7-*Dimethoxy*isoquinoline *methiodide* is formed when the base is mixed with methyl iodide. It is sparingly soluble even in hot alcohol, from which it separates on cooling in pale buff, glistening, anhydrous needles, m. p. *ca.* 256° (decomp.; corr.) (Found: I, 38·3. $C_{12}H_{14}O_2NI$ requires I, 38·4%).

Reduction of 6 : 7-*Dimethoxy*isoquinoline.—The pure base (4·8 g., m. p. 93°), alcohol (20 + 5 c.c.), concentrated hydrochloric acid (20 + 20 c.c.), and tin-foil (20 g.) were digested for 30 hours on the water-bath. The product was dissolved in hot water (0·7 litre) and freed from tin by hydrogen sulphide; on concentration, 5·22 g. of pure 6 : 7-dimethoxytetrahydro*iso*quinoline hydrochloride were obtained (in three crops). The mother-liquor was evaporated to dryness and mixed with alcohol, when 0·2 g. of the same salt, m. p. 260° after sintering from 256°, separated; the mother-liquor from this, when evaporated to dryness and mixed with absolute alcohol, deposited a further 0·05 g. (m. p. 242—245°; mixed with the pure salt, m. p. 252—258°). The total yield (5·47 g.) amounts to 94% of the theoretical. The final mother-liquor gave on evaporation to dryness a gummy residue (0·11 g.), from which no crystalline base or salt could be obtained.

6 : 7-*Dimethoxy*-1 : 2 : 3 : 4-*tetrahydro*isoquinoline *hydrochloride* crystallises from water in colourless quadrilateral plates, m. p. 262° (corr.). It is readily soluble in cold water, and very readily soluble in hot water, but sparingly soluble in cold alcohol (Found: C, 57·8; H, 7·2. $C_{11}H_{15}O_2N,HCl$ requires C, 57·5; H, 7·0%). The *picrate* crystallised from alcohol in broad, yellow needles, m. p. 202—203°

(corr.). The *base* (VII) crystallised from chloroform in colourless plates, which were easily soluble in chloroform, but sparingly soluble in ether. It readily takes up carbon dioxide from the air, and was not obtained free from carbonate (m. p. 80—130°).

6 : 7-Dimethoxytetrahydro*iso*quinoline was also obtained by the reduction of 6 : 7-dimethoxy-3 : 4-dihydro*iso*quinoline with tin and alcoholic hydrochloric acid. The hydrochloride and picrate from this source had the m. p.'s recorded above, alone or mixed with the corresponding salts from the reduction of 6 : 7-dimethoxy*iso*-quinoline.

Reduction of 6 : 7-*Dimethoxy*isoquinoline *Methiodide*.—The pure methiodide (10 g.), alcohol (40 c.c.), concentrated hydrochloric acid (40 + 20 c.c.), and tin-foil (20 + 5 g.) were digested for 18 hours on the water-bath, and the product was deprived of tin by means of hydrogen sulphide. The residue remaining after evaporation of the water was dissolved in water and mixed with picric acid (7 g.) in hot water (300 c.c.), when, on cooling, 10·45 g. of 6 : 7-dimethoxy-2-methyl-1 : 2 : 3 : 4-tetrahydro*iso*quinoline picrate, m. p. 158° (corr.), separated. The base (0·25 g.) regenerated from the mother-liquors was converted into picrate and gave 0·35 g. of the above salt, m. p. 152—153°. The total yield is thus 82% of the theoretical. The identity of the salt, for which Pyman (*loc. cit.*) gives m. p. 159—160° (corr.), was confirmed by the preparation from it of the hydrochloride, m. p. (dry) 217—218° (corr.), and base, m. p. 83—84° (corr.) (Pyman gives m. p. 216—217° [corr.] and 83—84° [corr.] respectively), and by comparison of the latter with an authentic specimen prepared by the reduction of 6 : 7-dimethoxy-3 : 4-dihydro*iso*quinoline methiodide (mixed m. p. 83—84° [corr.]).

We desire to thank (1) the Council of the Lord Kitchener National Memorial Fund for the grant of a scholarship which has enabled one of us (C. I. K.) to take part in the investigation, (2) Messrs. Brotherton and Co., Ltd., tar distillers, Leeds, for raw materials and facilities for the isolation of *iso*quinoline, (3) Professor R. Robinson, F.R.S., and Mr. H. S. Land, B.Sc.Tech., for gifts of *iso*quinoline, and (4) the Wellcome Chemical Research Laboratories for a specimen of 6 : 7-dimethoxy-3 : 4-dihydro*iso*quinoline.

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CCXXI.—*The Surface Tensions of Aqueous Phenol Solutions. Part II. Activity and Surface Tension.*

By Arthur Kenneth Goard and Eric Keightley Rideal.

The equation of Gibbs determining the surface adsorption of substances in solution ("Equilibrium in Heterogeneous Systems," Scientific Papers, Vol. II) should strictly be written in the form $\Gamma = -d\sigma/d\mu$, where σ = surface tension and $\mu = \mu_0 + RT \log_e a$. Γ is here the excess concentration (positive or negative) of the solute at the surface and a is the mean activity of the solute (compare Lewis and Randall, "Thermodynamics," New York, 1923).

Very little attempt has been made hitherto to apply this equation to actual cases, most workers having dealt with systems in which the activity can be equated approximately to the bulk concentration of the solute. Since it is frequently just in concentrated solutions, where this equality fails to hold, that adsorption phenomena become important, it is highly desirable that the strict form of the Gibbs equation should be more widely adopted. As a simple example of the use of activities, we may take the case of a binary liquid mixture at its critical solution temperature, where a small change in the relative proportions of the components does not affect the surface tension, regardless of the amount of surface adsorption (Lewis and Randall, *op. cit.*, Chap. XXI, Exercise 7). It further follows that in the region of this critical point, unless the adsorption exhibit very sudden and violent changes, the surface tension is largely independent of the relative concentrations of the two components. In Part I of this investigation it was shown that the difference between the surface tensions of the two liquid phases formed by phenol and water was only 0·33 dyne/cm. at 0°, and that this difference diminished continuously up to the critical solution temperature. The surface tensions of the two phases are thus remarkably similar, despite large differences of composition. A generalisation of this kind was stated empirically by Antonov in 1907 (*J. Chim. Phys.*, 1907, **5**, 364); it is now seen to be the natural result of the activity relations displayed by two liquids in the "critical zone."

As an example of the opposite kind, in which the activity of a solute may undergo great alteration without any change of concentration, we may take the "salting out" of organic substances from aqueous solutions by the addition of inorganic salts, *e.g.*, that of phenol by sodium chloride. Various experimenters have shown that the toxicity of phenol in aqueous solution is increased by the addition of salt; their results have been summarised by Lash Miller (*J. Physical Chem.*, 1920, **24**, 562). Berczeller (*Biochem. Z.*,

1914, **66**, 173, 191, 202) showed that this increase was accompanied by a lowering of the surface tension. Miller (*loc. cit.*) suggested that both these phenomena are due to an increase in the chemical potential of the phenol; and Lemon (*J. Physical Chem.*, 1920, **24**, 570) and Laird (*ibid.*, p. 664) showed that approximately the same toxic power was exhibited by all "equivalent" phenol solutions—*i.e.*, solutions of phenol in water containing different amounts of salt, but all in equilibrium with the same solution of phenol in some immiscible solvent (*e.g.*, kerosene).

A more precise investigation of the relation between the surface tensions and activities of such solutions being desirable, the system phenol–sodium chloride–water was chosen for this purpose. To determine the phenol activity in aqueous solutions containing salt, analysis of the vapour proved inadequate, the partial pressure of the phenol being too small to allow of accurate measurement, and a partition method in which amyl alcohol was used as the second solvent failed because the distribution of amyl alcohol itself was affected by the presence of salt. Paraffin oil, however, being nearly insoluble in water, was practically free from this disadvantage.

The concentration of phenol in paraffin in equilibrium with a saturated aqueous solution of the former is small (about 0·2 mole/litre). Unfortunately, from zero concentration up to fifth molar, the activity of phenol in paraffin is not directly proportional to the concentration (see Table I); otherwise, its determination would be very simple. Since phenol associates in water, the curve relating its activity in water to its concentration therein must be *concave* towards the concentration axis (*i.e.*, the activity increases more slowly than the concentration). The experimental curve relating the concentrations of phenol in paraffin in equilibrium to the corresponding concentrations in water was, however, *convex* towards the latter axis, showing, as might indeed have been anticipated, that phenol associates more rapidly in paraffin than in water.

An independent method of determining the phenol activity is therefore necessary in order that the concentrations of phenol in paraffin may be referred to the true activities of the former. From data supplied by Peddle and Turner (J., 1911, **99**, 691), it is possible to calculate the approximate activity of phenol in salt-free solution, up to 0·55*M*, if the effect due to heat of dilution be neglected. By referring these to the values in Table I, using a rough extrapolation to cover the higher phenol activities, we were able to draw a set of curves giving the relation between the concentration of phenol in the aqueous phase and the phenol activity. These curves were now initially concave towards the concentration axis.

Beyond a certain point, however, which corresponded to a 0·4*M*-

solution of phenol in pure water, the curves were inflected, becoming convex. This inflection was undoubtedly due to insufficient correction of the original data; at higher concentrations the effect of heat of dilution probably becomes of importance. Analysis of the freezing-point data by Lewis and Randall's method (constancy of j/m) also indicated that errors in the activity values might be expected to become considerable at concentrations much beyond the above. In particular, the graphical extrapolation necessary over the regions of higher activity is very sensitive to error.

It was decided, therefore, to assume that the activities, as calculated by the freezing-point method, were sensibly correct up to a value of about 0·3 (*i.e.*, that corresponding to a 0·4M-solution of phenol in pure water). Beyond this, the relation between activity and concentration was assumed to be expressed by a graphical extrapolation of each curve, preserving throughout the extrapolated region the curvature of its earlier portion. This procedure was in some measure justified (*a*) by the fact that for the curves relating to the higher salt concentrations the extrapolation was nearly linear, and (*b*) by the observation that if the corrected activities, as obtained separately from each of the curves, were all referred to a common diagram expressing the relation between phenol activity and concentration in paraffin solution, a set of points was obtained which lay, with very small deviations, on a single curve.

Finally, therefore, a smooth curve was drawn through these points, relating the concentration of phenol in paraffin to its corrected activity; and from this curve the values given in column IV of Table I were obtained. The results are shown in Fig. 1; curves I—VI give the activities of phenol in aqueous solutions containing 0, 5, 10, 15, 20, and 25 g. of sodium chloride per 100 c.c. of solution respectively. The nature of the second, graphical, correction of activities is shown in curve V, where the dotted curve indicates the inflection obtained at higher concentrations, using the extrapolation from the freezing-point data of Peddle and Turner.

The experimental procedure adopted to determine the partition of the phenol was as follows: 20 c.c. Portions of a phenol solution of known concentration were placed with 20 c.c. of paraffin oil in glass-stoppered bottles, to which weighed amounts of salt had been added, immersed in a thermostat at 20°. The mixtures were shaken vigorously and repeatedly for some hours, and 10 c.c. of the lower, aqueous, layer were then removed and the phenol content was estimated by Koppeschaar's method, using a standard solution of potassium bromate and bromide. The phenol content of the paraffin phase was estimated by difference, save in the case of those solutions which comprised *three-phase* mixtures: water + phenol +

salt, a phenol-rich phase, and phenol + paraffin. Of these mixtures, which are marked " saturated " in Table I, the aqueous phase was estimated as before; 10 c.c. of the paraffin phase were then removed, and shaken with an equal volume of water. From the amount of phenol passing into the water, it was possible, by means of previous measurements of the partition of phenol in the absence of salt, to estimate the amount of phenol present in the paraffin phase of the original mixture.

TABLE I.

Column I gives the concentration of sodium chloride in moles/litre; column Iα, the salt concentration in g./100 c.c. of solution.

Salt conc.		Phenol concentration (mole/litre).		IV. Corrected
I.	Iα.	II. In water.	III. In paraffin.	phenol activity.
0	0	0·069	0·014	0·067
		0·206	0·044	0·189
		0·419	0·098	0·345
		0·663	0·166	0·462
		0·889 (sat.)	0·228	0·526
0·855	5	0·064	0·019	0·090
		0·188	0·062	0·244
		0·304	0·111	0·374
		0·366	0·145	0·432
		0·510 (sat.)	0·265	0·550
1·71	10	0·059	0·024	0·110
		0·170	0·081	0·300
		0·214	0·111	0·374
		0·350 (sat.)	0·292	0·558
2·57	15	0·052	0·030	0·134
		0·147	0·103	0·356
		0·180	0·147	0·436
		0·236	0·281	0·556
3·42	20	0·046	0·036	0·158
		0·124	0·126	0·400
		0·146	0·179	0·476
		0·180	0·336	0·576
		0·182 (sat.)	0·353	0·580
4·28	25	0·040	0·043	0·180
		0·102	0·148	0·438
		0·114	0·211	0·508
		0·134	0·395	0·588

The Surface Tensions of Aqueous Phenol, and Phenol–Salt, Solutions.

In these experiments the phenol content was estimated by titration, and the surface tensions were determined by the drop-weight method, using the apparatus previously described (Goard and Rideal, this vol., p. 780). The densities of the solutions of sodium chloride were taken from Kohlrausch, the difference of density (which is small) due to the phenol being taken as directly proportional to the phenol concentration.

All measurements were made at 20°. The weight of ten drops

was ascertained, the mean weights given below being calculated from several closely concordant determinations.

Table II.

The first column gives the salt concentration in moles/litre, the second column the concentration in g./100 c.c. of solution.

Salt conc. I.	Salt conc. II.	Phenol conc. (mole/litre).	Mean wt. of 10 drops (g.).	Density.	Surface tension (dynes/cm.).
0	0	0·050	0·8442	0·999	67·88
		0·127	0·7473	0·999	60·10
		0·268	0·6398	1·000	51·58
		0·496	0·5550	1·003	44·97
		0·889	Surface tension taken from Part I		39·98
1·71	10	0·053	0·7988	1·064	64·26
3·42	20		0·7416	1·125	59·68
5·13	30		0·6749	1·182	54·61
6·15	36		0·6492	1·215	52·68
1·71	10	0·127	0·6811	1·065	55·14
3·42	20		0·6100	1·126	49·43
4·28	25		0·5616	1·154	45·32
4·70	27·5		0·5451	1·169	44·23
4·96	29		0·5452	1·180	44·18
1·71	10	0·223	0·5891	1·066	47·93
2·57	15		0·5489	1·097	44·48
2·98	17·5		0·5281	1·112	42·75
3·42	20		0·5243	1·127	42·50
0·85	5	0·344	0·5680	1·035	46·02
1·37	8		0·5449	1·053	44·15
2·05	12		0·5156	1·080	41·78
2·22	13		0·5121	1·086	41·59

In Fig. 2, the surface tensions of phenol solutions containing different amounts of salt (obtained by graphical means from Table II) are shown plotted against the logarithm of the corresponding phenol activities. Curves I—VI represent solutions containing 0, 5, 10 . . . 25 g. of salt per 100 c.c., respectively (corresponding thus to curves I—VI in Fig. I).

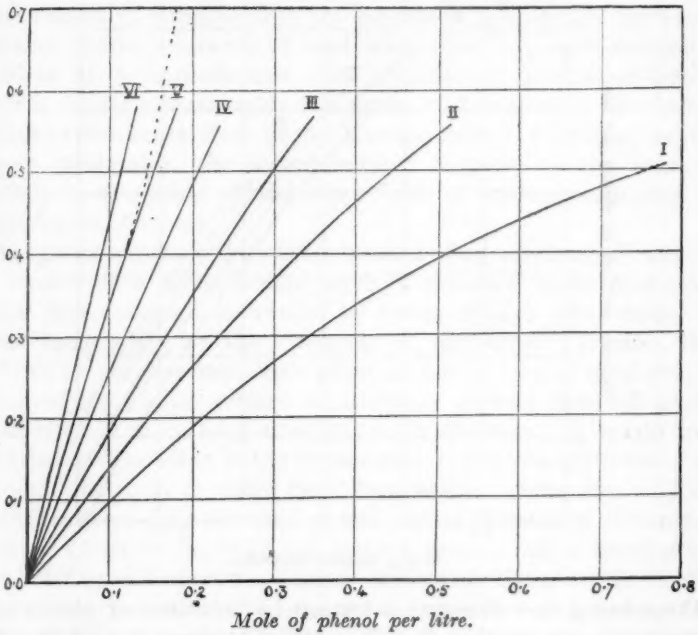
Considering first curve I, it will be observed that, as the activity of the phenol increases, the slope of the curve also increases, at first rapidly, then much more slowly, up to the point of saturation. The whole curve, in fact, strongly resembles those reproduced by Harkins for aqueous solutions of the lower fatty acids ("Surface Energy in Colloidal Systems," Chap. VI, Vol. I of "Colloidal Behaviour." Bogue, New York, 1924).

The maximum value of the adsorption, Γ, found by drawing a tangent to the curve at its steepest point, and taking the mean of several such determinations, is $69{\cdot}2 \pm 1 \times 10^{-11}$ g.-mol. per sq. cm. If we follow Langmuir (*J. Amer. Chem. Soc.*, 1917, **39**, 1848) in assuming that the surface layer is comprised in a unimolecular film, the area, A, occupied by a single molecule at the surface is

given by $A = 1/\Gamma N$, whence $A = 23{\cdot}8 \pm 0{\cdot}5 \times 10^{-16}$ sq. cm. The value found by Adam (*Proc. Roy. Soc.*, 1923, *A*, **103**, 676) in the cases of *p*-hexadecyl- and *p*-octadecyl-phenol was also 23·8 Å.U. This, he considers, represents the area of cross-section of the benzene nucleus. The agreement here can scarcely be accidental; it indicates that the molecules of ordinary phenol form a unimolecular film at the surface, the hydroxyl groups being drawn inwards, leaving the plane of the benzene nucleus at right angles to the surface.

FIG. 1.

Activity of phenol in aqueous solution.



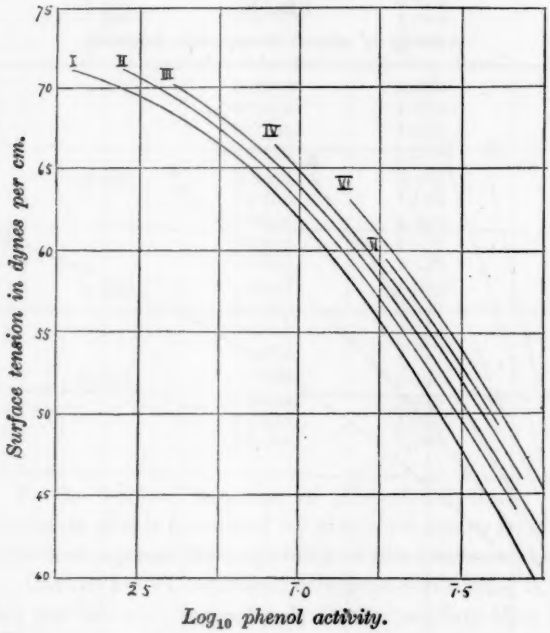
Mole of phenol per litre.

The thickness of the adsorbed layer can only be calculated by assuming a value for the density, which is probably nearly that of pure phenol. The density of solid phenol at 33° is 1·06; that of the phenol-rich phase formed at 20° is 1·05. The thickness of the adsorbed layer, taking the latter figure, is 6·4 Å.U. The probable length of the benzene ring is given by Adam as about 6 Å.U.

These values differ considerably from those given by Langmuir (*loc. cit.*), who, from data furnished by Morgan and Egloff (*J. Amer. Chem. Soc.*, 1916, **38**, 555, 844), deduces that the phenol molecule, of mean area 34 Å.U., lies flat on the surface of the solution. This difference is principally due to the fact that Langmuir assumed the

phenol activity to be throughout proportional to the concentration. If the present values for the surface tensions be plotted against the logarithms of the *concentrations*, the maximum apparent value of Γ is reached in the middle of the curve, at a concentration of phenol of about 0·2 mole/litre, after which there is a decrease of slope, and consequently a decrease in the apparent value of the adsorption, due to the fact that no allowance has been made for association of the phenol.

FIG. 2.



Considering now the curves formed by solutions of phenol containing salt, we see that they lie parallel to curve I, and have the same slope at corresponding activities. It follows that the amount of phenol adsorbed at the surface of equi-active phenol solutions is independent of the concentration of salt in the solution. The curves are, however, not coincident, showing that the salt has an effect on the actual value of the surface tension. The extent of the displacement of the curves shows this effect to be nearly the same as that of salt on pure water. At higher concentrations, however, the effect of salt on the phenol solutions diminishes, the curves for 15, 20, and 25% of salt being closer together than those for 0, 5, and 10%. With pure water, on the other hand, the effect increases as the salt solution becomes more concentrated.

Discussion of Results.

The results described in this paper do not seem to support the now well-known theory of surface tension proposed by Langmuir (*loc. cit.*) and Harkins (*op. cit.*), which maintains (1) that the surfaces of liquids containing asymmetric molecules consist of a unimolecular film of these molecules, oriented in such a way that their more active portions are drawn inwards, and (2) that " the surface energy of a liquid is thus not a property of the group molecules, but depends only on the least active portions of the molecules, and the manner in which these are able to arrange themselves in the surface layer " (Langmuir, *loc. cit.*). We have seen that there is good reason to suppose that the adsorbed layer at the surface of aqueous phenol solutions, at least when these approach saturation, consists of a unimolecular film of oriented phenol molecules. This is in accordance with the views of Langmuir; but further consideration must lead us to hesitate before ascribing, as this theory postulates, the actual surface tensions of the solutions entirely to the effect of the stray fields of force surrounding the outer layers of atoms.

Langmuir supposes the surface tension of an aqueous salt solution to consist of a unimolecular layer of oriented water molecules; but if these oriented molecules, by virtue of their stray fields, are alone responsible for the elevation of the surface tension, it is difficult to conceive that their effect should be largely unaltered by the presence at the surface of a closely packed layer of phenol molecules. Yet we have seen this to be the case. It would seem that, besides the effect of the surface film, it is necessary to take into account what may be called the " foundation " of the film. This is further indicated by the form of the curves obtained if the surface tensions given in Table II are plotted against salt concentration. The lowering of surface tension is at first nearly linear; with increasing salt concentration, the rate of fall increases somewhat up to a point of inflection, shortly after which a second phase separates; the surface tension varies very little beyond this point. Close inspection of the curves shows that there is no marked discontinuity at the " salting-out " point; for some little distance before the point is actually reached the rate of fall of surface tension diminishes, indicating possibly a thickening of the surface film of phenol molecules. Even here, however, the effect of the salt persists; since the actual value of the surface tension at different salting-out points varies with the salt concentration.

We must conclude, therefore, that although the presence of a unimolecular film of oriented phenol molecules at the surface is probably the chief factor in determining the surface tension,

the molecules at greater depths have also an influence upon it. Recent work by Iredale (*Phil. Mag.*, 1923, **45**, 1088; 1924, **48**, 177), Wilson (*Physical Rev.*, 1920, **16**, 8), and Terzaghi (*ibid.*, p. 54) indicates that molecular forces may be active over ranges considerably exceeding the length of a single molecule. A complete theory of surface tension should cover both the surface film and the "foundation" upon which that film rests.

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CCXXII.—*Bromination of Acyl Derivatives of Phenylhydrazine. Preparation of 2:4-Dibromophenylhydrazine.*

By JAMES ERNEST HUMPHRIES and ROY EVANS.

BROMINATION, even with excess of the halogen, of the acetyl and benzoyl derivatives of phenylhydrazine in cold chloroform or carbon tetrachloride does not produce diazonium salts (compare Michaelis, *Ber.*, 1893, **26**, 2190; Vaubel, *J. pr. Chem.*, 1894, **49**, 540; 1897, **55**, 220). The formation of diazonium salt in Michaelis's experiment appears to have been due to the action of the bromine on phenylhydrazine formed from its acetyl derivative by hydrolysis by the hydrochloric acid used as solvent.

In our experiments, no evidence was obtained of the existence of *N*-bromo-compounds, proved by Chattaway (J., 1908, **93**, 852) to be formed in the bromination of phenylhydrazine.

The experiments were carried out at −5° to −10°. After the initial experiments chloroform was used as solvent, since the acyl derivatives are more soluble in it than in carbon tetrachloride. The brominated phenylhydrazines produced were identified by conversion into the bromophenylhydrazones of benzophenone or benzaldehyde. Tests for diazonium compounds were carried out with an alkaline solution of β-naphthol.

Acetylphenylhydrazine. (1) Bromine (1 mol.) was added gradually to the solution, which became red and turbid. *Acetyl-p-bromophenylhydrazine hydrobromide* slowly separated as a white, crystalline solid, m. p. 132° (decomp.) (Found: total Br, 51·5; HBr, by titration with baryta, 26·4. $C_8H_9ON_2Br,HBr$ requires total Br, 51·6; HBr, 26·1%). The compound dissolved immediately in alcohol and from the solution acetyl-*p*-bromophenylhydrazine, m. p. 164°, was soon deposited (Found: Br, 34·7. Calc., Br, 34·9%).

(2) A solution of 12 g. (1 mol.) of acetylphenylhydrazine in 400 c.c. of chloroform was cooled to 0°, slowly treated with 8·2 c.c. (2 mols.) of bromine, and kept for 12 hours at the ordinary temperature, when the heavy, red oil that had separated solidified (from more dilute solutions it separated in crystals). The crystalline mass, which was washed with chloroform, was *acetyl-2 : 4-dibromophenylhydrazine hydrobromide*, m. p. 146° (decomp.); it decomposed in the air, giving off hydrogen bromide (Found: total Br, 61·85; HBr, 20·9. $C_8H_8ON_2Br_2,HBr$ requires total Br, 61·7; HBr, 20·8%). The compound was dissolved in cold alcohol and water added to the solution, when acetyl-2 : 4-dibromophenylhydrazine, m. p. 146°, was formed in theoretical yield (24—25 g.) (Found: Br, 51·7. Calc., Br, 51·9%). The hydrochloride of the hydrazine was easily obtained by warming the acetyl derivative with concentrated hydrochloric acid.

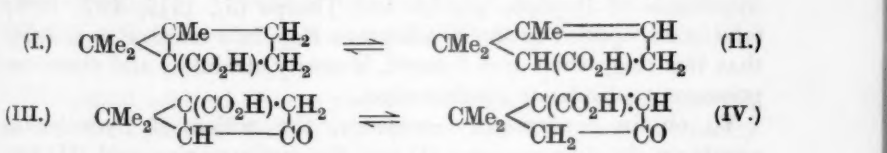
Benzoylphenylhydrazine. The solution turned red and turbid when the bromine (2 mols.) was added and after a short time white needles of 2 : 4-dibromophenylhydrazine hydrobromide separated (Found: Br, 68·9. Calc., Br, 69·2%).

THE UNIVERSITY, ABERDEEN. [*Received, May 21st*, 1925.]

CCXXIII.—*The Structure of α-Campholytic Acid. A Correction.*

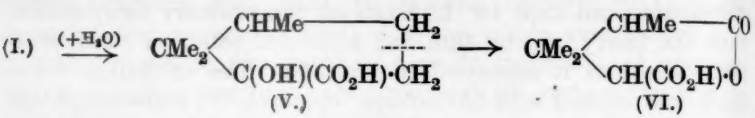
By JUAN PEDIGE CHARLES CHANDRASENA, CHRISTOPHER KELK INGOLD, and JOCELYN FIELD THORPE.

IN a previous paper (J., 1922, **121**, 1542) it was pointed out that the existing evidence of the structure of campholytic acid is equivocal: it could be used just as easily to support the bridged-ring constitution (I) as the accepted unsaturated structure (II). The possibility of a tautomeric form having structure (I) had not previously been considered, but it was suggested that the time had arrived to do so in view of the proved tautomerism between (III) and (IV) (compare Parts I and II of the same series).

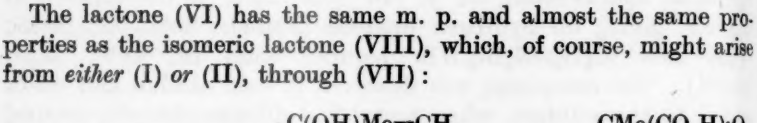


The object of the paper was, therefore, to advance unequivocal evidence favouring formula (I), and it was suggested that the oxid-

ation of campholytic acid to the lactonic acid (VI) might be regarded in that light:



The lactone (VI) has the same m. p. and almost the same properties as the isomeric lactone (VIII), which, of course, might arise from *either* (I) *or* (II), through (VII):



The lactone actually obtained, however, is not (VI), as was at first supposed, but (VIII); and so, again, the evidence of structure is ambiguous.

Structure (VI) was incorrectly assigned to the lactonic acid on the grounds of its identity with a specimen prepared from trimethylglutaric acid by Pandya and Thorpe (J., 1923, **123**, 2865), who, being misled by an erroneous statement of Balbiano (now corrected: this vol., p. 1072), wrongly regarded the substance as possessing formula (VI). The authors desire to express their regret that this mistake should have arisen.

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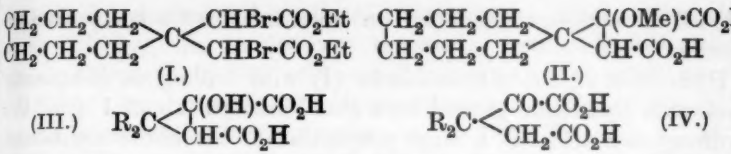
THE UNIVERSITY, LEEDS. [*Received, June 3rd*, 1925.]

CCXXIV.—*The Formation and Stability of* spiro-*Compounds. Part XII. Further Evidence for the Multiplanar Configuration of the* cyclo*Heptane Ring.*

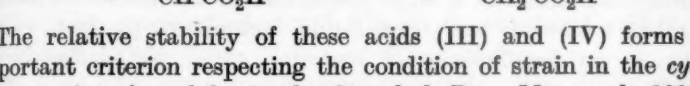
By JOHN WILLIAM BAKER.

BAKER and INGOLD showed (J., 1923, **123**, 122) that the original hypothesis of Beasley, Ingold, and Thorpe (J., 1915, **107**, 1080) fails, when applied to the *cyclo*heptane ring, in a manner suggesting that this ring, when once formed, is nearly strainless and therefore possesses multiplanar configuration.

To obtain confirmatory evidence, the action of hydrolysing agents on the dibromo-ester (I) and the methoxy-ring acid (II) has been investigated with the object of preparing either or both of the acids of types (III) or (IV).



(I.) (II.)

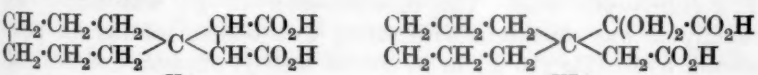


(III.) (IV.)

The relative stability of these acids (III) and (IV) forms an important criterion respecting the condition of strain in the *cyclo*heptane ring, for whilst in the dimethyl ($R_2 = Me_2$, angle 109·5°) and *cyclo*pentane series ($R_2 = C_4H_8>$, angle 108°) the open-chain keto-form is the stable modification, in the *cyclo*hexane series ($R_2 = C_5H_{10}>$, angle 120°) the strain in the three-membered *spiro*-ring is so far relieved that the hydroxy-ring acid becomes the stable isomeride; in intermediate cases, $R_2 = Et_2$ and Pr^n_2, a tautomeric equilibrium exists between the keto- and hydroxy-ring forms. If, therefore, the *cyclo*heptane ring is uniplanar as used to be supposed (angle 128·6°), its hydroxy*cyclo*propane compound of type (III) should be even more stable than the *cyclo*hexane analogue. If, on the other hand, the seven-membered ring is multiplanar, and therefore strainless or nearly so, it should resemble more closely its *cyclo*pentane analogue and the keto-acid (type IV) should be the stable modification.

The results obtained clearly indicate that the *cyclo*heptane ring is strainless, or nearly so,* for the open-chain keto-acid was the more stable isomeride, the hydroxy-ring acid (which was isolated) passing into the keto-acid under the conditions in which this reversible isomeric change has been observed in other cases.

On hydrolysis of the dibromo-ester (I) with boiling methyl-alcoholic potassium hydroxide the methoxy-ring acid (II), analogous in all respects to the corresponding *cyclo*hexane compound, was obtained. On hydrolysis with hydrobromic acid this methoxy-ring acid gave a large yield of a liquid acid and a very small yield of a solid acid which, although insufficient was obtained for analysis, was identified as *cyclo*heptane*spirocyclo*propane-1 : 2-dicarboxylic acid (V), the hydrobromic acid evidently having acted partly as a reducing agent.



(V.) (VI.)

The liquid acid, which was purified through its silver salt, proved to be the hydrated form (VI) of the keto-acid, for it readily

* Other investigators have reached the same conclusions on quite different grounds (compare Meerwein and his collaborators, *J. pr. Chem.*, 1922, **104**, 161, 289; Dickens, Horton, and Thorpe, J., 1924, **125**, 1830).

yielded a semicarbazido-acid on treatment with semicarbazide acetate.*

Hydrolysis of the dibromo-ester (I) with boiling 64% aqueous potassium hydroxide yielded (*a*) a small amount (about 1%) of the hydroxy-ring acid, (*b*) a large proportion of the above-mentioned hydrated keto-acid, and (*c*) a liquid lactonic by-product which, owing to an insufficiency of material, could not definitely be identified.

From these experiments, it appears that, in the presence of hot concentrated alkalis, a tautomeric equilibrium, greatly favouring the open-chain form, exists between the hydroxy-ring acid and the keto-acid.

Thus the *cyclo*heptane compounds resemble closely their *cyclo*pentane analogues, which contain a practically strain-free ring, and therefore it may be asserted with considerable confidence that the *cyclo*heptane ring also is nearly strainless as suggested in the earlier communication (*loc. cit.*).

It seems curious that the *cyclo*heptane ring should be multiplanar whilst the *cyclo*hexane ring shows no evidence of strainless configuration until joined to another ring in some such combination as is represented in decahydronaphthalene. This, however, can be accounted for if we assume with Mohr (*J. pr. Chem.*, 1918, **98**, 352) that these rings undergo vibrational interchange between the strainless and uniplanar phases, and further postulate that the uniplanar phase, which is more highly strained in the *cyclo*heptane than in the *cyclo*hexane series, is, for that reason, of much smaller duration in the former than in the latter type of ring.

Experimental.

The ethyl $\alpha\alpha'$-dibromo*cyclo*heptane-1 : 1-diacetate used was prepared as described by Baker and Ingold (*loc. cit.*). Since it cannot be distilled without passing into the bromolactone, the undistilled product was employed.

Hydrolysis of the Dibromo-ester (I).—(a) *With methyl-alcoholic potassium hydroxide.* cyclo*Heptane*spiro-1-*methoxy*cyclo*propane*-1 : 2-*dicarboxylic acid.* The dibromo-ester (5 g.) was added as rapidly as was consistent with safety to a boiling solution of potassium hydroxide (10 g.) in 30 c.c. of methyl alcohol, and boiling

* Incidentally an observation was made which probably explains the frequent failure to prepare semicarbazones of the ketoglutaric acids previously investigated. The *cyclo*heptane semicarbazido-acid is a stronger acid than acetic acid and under the ordinary conditions of semicarbazone formation takes sodium from the sodium acetate employed. Its mono- and di-sodium salts are sufficiently sparingly soluble to separate from the solution, but it may well be that in lower series such salts are too soluble to do likewise.

continued under reflux for a further 20 minutes. After evaporation of the alcohol, the residue was repeatedly extracted with ether, whence the methoxy-ring acid was obtained as a gum which slowly solidified. On crystallisation from ether–ligroin (b. p. 40—60°), it was obtained in large rosettes, m. p. 165° (Found: C, 58·7; H, 7·4; *M*, by titration, 121·3. $C_{12}H_{18}O_5$ requires C, 59·4; H, 7·5%; *M*, 121·1).

(b) *With* 64% *aqueous potassium hydroxide.* The dibromo-ester (5 g.) was added as rapidly as was consistent with safety to 45 c.c. of boiling 64% potash solution, and boiling continued for 20 minutes. The residue obtained from the ethereal extract of the cooled, diluted, and acidified product was a gum which was repeatedly extracted with warm water. The aqueous extract on evaporation left an almost colourless gum, from which a minute quantity of the hydroxy-ring acid (III) was slowly deposited as a white, crystalline solid (mixed m. p. determination).

The liquid fraction of the soluble portion, treated with semicarbazide hydrochloride in a saturated solution of sodium acetate, slowly deposited the white *disodium* salt of the semicarbazido-acid, which was drained on porous tile and crystallised from methyl alcohol–ethyl acetate, from which it separated as a crystalline powder, decomp. 240° (Found: Na, 14·3. $C_{12}H_{17}O_5N_3Na_2$ requires Na, 14·0%). Another portion of the gum was dissolved in dilute ammonia and the *silver* salt precipitated by the addition of silver nitrate to the neutral solution (Found: Ag, 46·8. $C_{11}H_{16}O_6Ag_2$ requires Ag, 46·9%).

The portion insoluble in water formed no semicarbazone derivative and from its general characteristics appeared to be the same hydroxy-lactone obtained when the bromo-lactone was hydrolysed with concentrated potash solution (Baker and Ingold, *loc. cit.*).

Hydrolysis of the Methoxy-ring Acid with Hydrobromic Acid.—*αα′-Dihydroxy*cyclo*heptane*-1 : 1-*diacetic acid* (VI). The methoxy-ring acid (0·75 g.) was heated under reflux with 7·5 c.c. of hydrobromic acid (*d* 1·49) for 2 hours, the hydrobromic acid evaporated off on the steam-bath, and the residue extracted with ether. The gum obtained from the ethereal extract deposited, after long standing, a small quantity of a crystalline acid, m. p. 215°, which depressed the m. p. of the hydroxy-ring acid but not that of the *cyclo*heptane *spiro*acid (V).

The portion which would not solidify, consisting of the hydrated form of the keto-acid, was dissolved in dilute ammonia, silver nitrate solution added to the neutral solution, and the precipitated *silver* salt (Found: Ag, 46·7. $C_{11}H_{16}O_6Ag_2$ requires Ag, 46·9%) washed successively with water, alcohol, and ether. The acid was

regenerated by warming the silver salt with hydrochloric acid and extracting with pure ether. On treatment with a solution of semicarbazide acetate, it deposited the white, crystalline *monosodium* salt of the semicarbazido-acid, which, treated like the disodium salt, was obtained as a white, crystalline powder, decomp. 235° [Found: C, 47·2 (corrected for the percentage of carbon which remained unburnt as sodium carbonate); H, 5·85; Na, 7·4. $C_{12}H_{18}O_5N_3Na$ requires C, 47·0; H, 5·9; Na, 7·5%].

A Correction.—The acid X (this vol., p. 987), described as a *bicyclo*heptane derivative, has since been found to be a lactonic acid derived from this by hydrolytic fission of the three-membered ring. The mechanism of the reaction is being further investigated.

The author desires to express his gratitude to Professor C. K. Ingold, F.R.S., for his kindly interest and advice during the progress of this investigation, and to the Research Fund Committee of the Chemical Society for a grant by which most of the expenses incurred in this research were met.

THE UNIVERSITY, LEEDS. [*Received, May 27th,* 1925.]

CCXXV.—*Tridentate Groups in Complexes of Tetrahedral and Octahedral Symmetry.*

By J. D. MAIN SMITH.

UNTIL 1912, the property of rotating the plane of propagation of polarised light had been invariably ascribed to the presence of "asymmetric atoms" in the molecules of compounds. In every case, each such characteristic atom was discernible as in direct association with four different atoms or atomic groups arranged tetrahedrally about the active atom. In 1911, Werner showed that optically active compounds could contain an "asymmetric atom" with which six atoms or atomic groups were octahedrally associated. His demonstration in 1912 of the existence of optically active compounds containing a cobalt atom octahedrally associated with three identical groups of atoms (chelate ethylenediamine molecules) led him to abandon the conception that optical activity is due to the presence of "asymmetric *atoms*" and to attribute optical activity to *molecular* asymmetry. Subsequent chemical evidence points strictly to the existence in optically active compounds generally, not of asymmetric atoms, but of asymmetric molecules, and, in the light of recent knowledge of the structure of atoms, it appears probable that every atom, at least so far as the outer structure is

concerned, possesses at least one plane of symmetry. Nevertheless, it is possible to discern in the molecule of every known optically *active* compound a central or nuclear atom about which the *asymmetry* of the molecule is focussed. This nuclear atom is the so-called asymmetric atom. In the case of optically *inactive* compounds, it is similarly possible to discern a central or nuclear atom about which the *symmetry* of the molecule is focussed. This atom, almost invariably that directly combined with the largest number of atoms or atomic groups, is the nuclear atom of Werner's co-ordination theory.

For the purposes of classification and nomenclature of chemical compounds it is necessary to select certain atoms in molecules as points of reference to which all other atoms in the molecule may be regarded as related. As the spatial relationships of atoms in molecules can be ascertained almost solely from considerations of symmetry, it is necessary to select the nuclear atom of a co-ordination complex as the point of reference, and to regard separately each atom directly attached thereto. An atom directly attached to a nuclear atom may itself be multivalent and may become the end member of an atomic group which may be considered as an entity or radical directly attached to the nuclear atom. Obviously such an atomic group may be attached directly to the nuclear atom by means of more than one atom, and atomic groups may thus be classified as unitary, chelate, and tridentate, respectively, according as they contain one, two, and three atoms directly attached to the nuclear atom.

The term "chelate group," used by Professor G. T. Morgan to indicate its claw-like attachment to a nuclear atom to form a cyclic system of linked atoms, may logically be extended to any atomic group which combines with a single atom to form a cyclic system, but it is convenient to restrict its use to those groups which yield heterocyclic systems when combined with nuclear atoms, usually metallic atoms.

Tridentate groups may be regarded as comprising three fused chelate groups and may be symbolised as ABC to indicate the three comprised chelate groups AB, AC, BC. Tridentate groups may be classified according to the number of different chelate groups comprised, and can be of only three types symbolised by AAA, AAB, and ABC, the first comprising three similar chelate groups, the second two similar chelate groups, and the third three different chelate groups.

Tridentate groups have long been known in organic chemistry, but invariably associated with so-called tetrahedral atoms. Removal of one of the median carbon atoms of naphthalene, for example,

leaves a typical tridentate group. Tridentate groups in inorganic chemistry were first identified by Werner in association with an octahedral nuclear atom, or more properly, with a nuclear atom having the co-ordination number six. The group $(NH_3)_3Co(OH)_3$, for example, was proved to be capable of uniting with another nuclear cobalt atom, both having the co-ordination number six, as in the complex ion

$$(NH_3)_3Co\begin{matrix}OH\\OH\end{matrix}Co(NH_3)_3,$$

in which each $(NH_3)_3Co(OH)_3$ group is a tridentate group to the other Co atom. Prior to 1924, all the tridentate groups identified were found in complexes containing at least two octahedral nuclear atoms, as in the foregoing example. In that year, Pope and Mann (*Compt. rend.*, 1924, **178**, 2085) proved that $\alpha\beta\gamma$-triaminopropane was a group capable of triple attachment to a single metallic atom having the co-ordination number six, the cobaltic and rhodium compounds containing only two molecules of the tri-acidic base per metallic atom.

In view of the interest attaching to such compounds containing tridentate groups in uni-nuclear octahedral complexes, the results of the examination some years ago of the possibilities of tetrahedral and octahedral isomerism, due to association of tridentate groups with a single nuclear atom, are now published. A complete examination of the possibilities of tetrahedral and octahedral isomerism in complexes containing single atoms or unitary groups and also those containing chelate groups has already been published ("Chemistry and Atomic Structure," 1924, ch. VII). The following tables are based on the system of symbolisation there presented, with the necessary modifications for tridentate groups.

Only one main type of tetrahedral complex containing tridentate groups is possible, and consists of one tridentate group (symbolised by three capitals) and one unitary group (symbolised by lower-case letters). As shown above, only three variants of tridentate groups are possible, symbolised by AAA, AAB, and ABC, to indicate the various possible combinations of three fused chelate groups. This single type of tetrahedral complex is thus divisible into only three classes, (i) AAAb, (ii) AABc, and (iii) ABCd. The first class consists of a single optically inactive form, and the second and third each of two optically active (enantiomorphous) isomerides.

Three main types of octahedral complexes containing tridentate groups are possible, the first containing three single atoms or three unitary groups, the second containing one chelate group (indicated by two capitals) and one single atom or unitary group, and the third

containing two tridentate groups. Three single atoms or three unitary groups considered together can have only three variants, symbolised by aaa, aab, and abc. There can thus be no more than nine variants of one tridentate group with three unitary groups, and no more than nine variants of two tridentate groups. These two sets each of nine classes are shown in Table 1. As chelate groups can be of no more than two variants, symbolised by AA and AB, there can be no more than six variants of one tridentate group with one chelate group and one unitary group. These six classes are also shown in Table 1. The octahedral configuration containing tridentate groups can thus give rise to no more than three main types comprising 24 separate classes.

The various possible isomeric forms of any one class are differentiated into *cis*- and *trans*-forms according to whether the tridentate group is attached to three adjacent points forming a triangle on an imaginary octahedron about the nuclear atom or to three points two of which are octahedrally polar. In the *cis*-configuration the nuclear atom lies outside and in the *trans*-configuration within the plane containing the tridentate group.

With one exception, every optically inactive form containing a tridentate group contains at least one plane of symmetry. The exception is in the case of the inactive *cis*-form of the combination ABC ABC, which contains a centre of symmetry. This configuration is unique in that it is the sole inactive form of the 430 octahedral forms so far examined (75 with only unitary groups, 206 with chelate groups, and 149 with tridentate groups) which does not contain a plane of symmetry.

The following tables relate only to complexes which contain one nuclear atom, but the correct number of isomerides even for binuclear cases may be simply deduced by aid of the tables. If a tridentate group, or the chelate group, or a unitary group contain a nuclear atom so that the group as a whole is asymmetric, *i.e.*, not superposable on its mirror-image, every form shown in the tables as optically inactive will be optically active and an enantiomorphous form will be possible. The number representing the inactive forms is thus simply doubled and added to the number of active forms. Only one other special case need be considered. If in the combination ABC DEF, the tridentate groups are each asymmetric and in addition are mirror-images of one another, the number of possible optically active *cis*-forms will be reduced by two and one optically inactive form will take their place and will, like the inactive *cis*-combination ABC ABC, contain a centre of symmetry.

To illustrate the use of the tables in the determination of the number of possible isomeric forms of uni-nuclear complexes con-

taining tridentate groups, the compounds containing triaminopropane may be taken. This tridentate group comprises three chelate groups, of which two are similar, and the symbol for the group is thus AAB. The compounds prepared contained two tridentate groups per metallic atom, and thus belong to type 3,

TABLE I.

Types and Classes of Octahedral Symmetry.

	One tridentate group and		Two tridentate groups.
	No chelate group.	One chelate group.	
Class.	Type 1.	Type 2.	Type 3.
(i)	AAA bbb	AAA b CC	AAA AAA
(ii)	AAA bbc	AAA b CD	AAA BBB
(iii)	AAA bcd	AAB c DD	AAA BBC
(iv)	AAB ccc	AAB c DE	AAA BCD
(v)	AAB ccd	ABC d EE	AAB AAB
(vi)	AAB cde	ABC d EF	AAB CCD
(vii)	ABC ddd	—	AAB CDE
(viii)	ABC dde	—	ABC ABC
(ix)	ABC def	—	ABC DEF

TABLE II.

Isomeric Forms of Type 1 *with One Tridentate Group and No Chelate Group.*

	Optically active.			Optically inactive.			
Classes of type 1.	Cis.	Trans.	Total.	Cis.	Trans.	Total.	Grand Total.
(i) AAA bbb	—	—	—	1	1	2	2
(ii) AAA bbc	—	—	—	1	2	3	3
(iii) AAA bcd	2	—	2	—	3	3	5
(iv) AAB ccc	—	—	—	1	1	2	2
(v) AAB ccd	2	—	2	1	2	3	5
(vi) AAB cde	6	—	6	—	3	3	9
(vii) ABC ddd	2	—	2	—	1	1	3
(viii) ABC dde	6	2	8	—	1	1	9
(ix) ABC def	12	6	18	—	—	—	18
Totals	30	8	38	4	14	18	56

TABLE III.

Isomeric Forms of Type 2 *with One Tridentate Group and One Chelate Group.*

	Optically active.			Optically inactive.			
Classes of type 2.	Cis.	Trans.	Total.	Cis.	Trans.	Total.	Grand Total.
(i) AAA b CC	—	—	—	1	1	2	2
(ii) AAA b CD	2	—	2	—	2	2	4
(iii) AAB c DD	2	—	2	1	1	2	4
(iv) AAB c DE	6	—	6	—	2	2	8
(v) ABC d EE	6	2	8	—	—	—	8
(vi) ABC d EF	12	4	16	—	—	—	16
Totals	28	6	34	2	6	8	42

TABLE IV.

Isomeric Forms of Type 3 *with Two Tridentate Groups.*

Classes of type 3.	Optically active.			Optically inactive.			Grand Total.
	Cis.	Trans.	Total.	Cis.	Trans.	Total.	
(i) AAA AAA	—	—	—	1	1	2	2
(ii) AAA BBB	—	—	—	1	1	2	2
(iii) AAA BBC	—	—	—	1	1	2	2
(iv) AAA BCD	2	—	2	—	1	1	3
(v) AAB AAB	2	—	2	1	1	2	4
(vi) AAB CCD	2	—	2	1	1	2	4
(vii) AAB CDE	6	—	6	—	1	1	7
(viii) ABC ABC	10	2	12	1	—	1	13
(ix) ABC DEF	12	2	14	—	—	—	14
Totals	34	4	38	6	7	13	51

class (v), AAB AAB. Reference to Table IV shows that this class represents four isomeric forms, two optically active (enantiomorphous, *cis*-forms, one inactive *cis*-form, and one inactive *trans*-form. Pope and Mann's compounds may thus have been one or both of the inactive forms, the mixture (racemoid) of active forms, or a mixture of the racemoid forms with either or both of the inactive forms.

The results of the examination of the types, classes, and isomeric forms of tetrahedral and octahedral complexes containing a group contributing four to the co-ordination number of a nuclear atom will be communicated later, conclusive evidence having been obtained in these laboratories of the existence of a quadridentate group in both octahedral and tetrahedral complexes.

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[*Received, May 12th,* 1925.]

CCXXVI.—*The Action of Halogens upon* m- *and* p-*Nitrobenzaldehydephenylhydrazones.*

By FREDERICK DANIEL CHATTAWAY and ARTHUR JOHN WALKER.

THE action of chlorine upon some arylhydrazones has been shown (Bülow, *Ber.*, 1918, **51**, 399) to result in the complete disruption of the hydrazone molecule and the formation of a diazonium chloride. This result might have been expected, since it had already been shown (Chattaway, J., 1908, **93**, 852; 1909, **95**, 958, 1065) that diazonium chlorides are produced quantitatively by the action of chlorine on arylhydrazines.

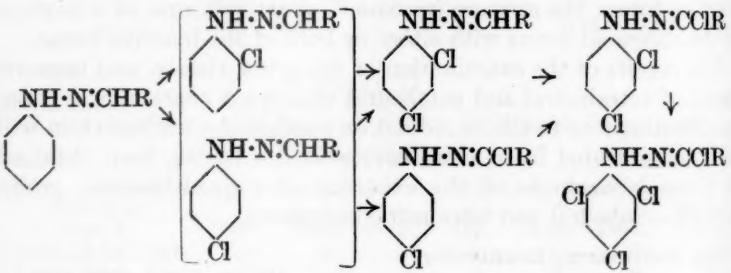
The stable nature of the nitrobenzaldehydephenylhydrazones renders it possible to follow more closely the action of chlorine upon them, since no appreciable breaking down of the molecule takes place during chlorination at the ordinary temperature.

When chlorine is passed in excess into a fine suspension in chloroform of *m*- or *p*-nitrobenzaldehydephenylhydrazone, the final product in each case is a tetra-substituted hydrazone, containing chlorine in the 2 : 4 : 6-positions of the hydrazine residue and also in the ω-position of the aldehyde residue:

$$C_6H_2Cl_3\cdot NH\cdot N{:}CCl\cdot C_6H_4\cdot NO_2.$$

If the chlorination be effected slowly, at various stages compounds can be isolated, the constitutions of which show that substitution in the two parts of the hydrazone molecule follows a similar course to that taken when acetanilide and benzaldehyde, respectively, are chlorinated.

Substitution in the ω-position of the aldehyde residue probably occurs to some extent from the first, but becomes more and more predominant as halogen enters the hydrazine nucleus. The main course of the substitution may be represented as follows, compounds not actually isolated being written in brackets (R = $C_6H_4\cdot NO_2$):



As might be expected, the situation of the nitro-group in the aldehyde residue somewhat affects the course of the reaction, the chlorine entering the ω-position more easily when the nitro-group occupies the para-position.

As in the chlorination of the acetarylamides, the chlorine probably first replaces the hydrogen of the imino-group, and becomes transferred to the nucleus by a process of intramolecular rearrangement. These transformations must take place with great ease, for the product of the action of an excess of hypochlorous acid upon *m*-nitrobenzaldehydephenylhydrazone in the presence of potassium bicarbonate gives all the reactions of a nitrogen chloride and is very probably a mixture of ω-*chloro*-m-*nitrobenzaldehydechloroimino*-o- and -p-*chlorophenylhydrazones*, since on warming with hydrochloric acid it yields ω-*chloro*-m-*nitrobenzaldehyde*-2 : 4-*dichlorophenylhydrazone*.

All the ω-chloro-*m*- and -*p*-nitrobenzaldehydechlorophenylhydrazones, when heated with sodium acetate and acetic acid, are converted quantitatively into α-*acetyl*-β-*nitrobenzoylchlorophenyl*-

hydrazines identical with the compounds obtained by acetylating the corresponding nitrobenzoylchlorophenylhydrazines; *e.g.*,

$$C_6H_3Cl_2\cdot NH\cdot N{:}CCl\cdot C_6H_4\cdot NO_2 \xrightarrow{CH_2\cdot CO_2Na} C_6H_3Cl_2\cdot NAc\cdot NH\cdot CO\cdot C_6H_4\cdot NO_2.$$

The α-acetyl-β-nitrobenzoyl-*p*- and -2:4-dichlorophenylhydrazines, when heated with concentrated hydrochloric acid, are readily and completely hydrolysed into acetic acid, *m*- or *p*-nitrobenzoic acid, and the corresponding *p*- or 2 : 4-dichlorophenylhydrazine; *e.g.*,

$$C_6H_3Cl_2\cdot NAc\cdot NH\cdot CO\cdot C_6H_4\cdot NO_2 \xrightarrow{H_2O} CH_3\cdot CO_2H + C_6H_3Cl_2\cdot NH\cdot NH_2 + NO_2\cdot C_6H_4\cdot CO_2H.$$

Under similar conditions the corresponding α-acetyl-*m*- or -*p*-nitrobenzoyl-2 : 4 : 6-trichlorophenylhydrazine is not hydrolysed completely as might be expected, but yields *m*- or *p*-nitrobenzoic acid, and α-acetyl-2 : 4 : 6-trichlorophenylhydrazine, which is not easily broken down further; *e.g.*,

$$C_6H_2Cl_3\cdot NAc\cdot NH\cdot CO\cdot C_6H_4\cdot NO_2 \xrightarrow{H_2O} C_6H_2Cl_3\cdot NAc\cdot NH_2 + NO_2\cdot C_6H_4\cdot CO_2H.$$

It seems probable that the firm attachment of the acetyl group in these compounds is to be attributed to the steric effect of the two *o*-substituted halogen atoms.

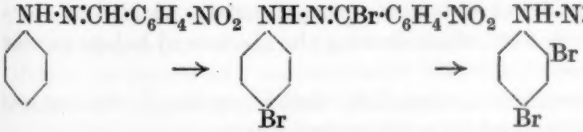
All ω-chloro-*m*- and -*p*-nitrobenzaldehydephenylhydrazones react with ammonia, forming *hydrazidines* by the replacement of the ω-chlorine atom by the amino-group; *e.g.*,

$$C_6H_2Cl_3\cdot NH\cdot N{:}CCl\cdot C_6H_4\cdot NO_2 \xrightarrow{NH_3} C_6H_2Cl_3\cdot NH\cdot N{:}C(NH_2)\cdot C_6H_4\cdot NO_2.$$

These are yellow or deep red basic compounds which all form colourless, well-crystallised hydrochlorides.

The action of bromine is similar to that of chlorine, although less energetic, direct substitution only leading to the introduction of two halogen atoms into the hydrazine residue, thus:

$$NH\cdot N{:}CH\cdot C_6H_4\cdot NO_2 \rightarrow NH\cdot N{:}CBr\cdot C_6H_4\cdot NO_2 \rightarrow NH\cdot N{:}CBr\cdot C_6H_4\cdot NO_2.$$



ω-*Bromo*-m- and -p-*nitrobenzaldehyde*-2 : 4 : 6-*tribromophenylhydrazones* are, however, easily obtained by the direct bromination of *m*- and *p*-nitrobenzaldehyde-2 : 4 : 6-tribromophenylhydrazones.

The behaviour of the ω-bromo-*m*- and -*p*-nitrobenzaldehyde-bromophenylhydrazones towards acetic acid and sodium acetate, and of the α-acetyl-β-nitrobenzoylbromophenylhydrazines towards hydrochloric acid, is exactly like that of the corresponding chloro-compounds.

The direct chlorination or bromination of any of the *m*- or *p*-nitrobenzaldehyde halogen-substituted phenylhydrazones naturally leads to the formation of an ω-substituted derivative; *e.g.*,

$$C_6H_4Cl\cdot NH\cdot N{:}CH\cdot C_6H_4\cdot NO_2 \xrightarrow{Br} C_6H_4Cl\cdot NH\cdot N{:}CBr\cdot C_6H_4\cdot NO_2.$$

The ω-bromo-*m*- and -*p*-nitrobenzaldehydebromophenylhydrazones react with ammonia, forming *hydrazidines*, which are mostly deep red, basic compounds, which yield colourless salts.

Experimental.

Action of Chlorine upon m-*Nitrobenzaldehydephenylhydrazone.*

Unless effected cautiously, chlorination of *m*-nitrobenzaldehydephenylhydrazone resulted only in the separation of the final product, ω-*chloro*-m-*nitrobenzaldehyde*-2 : 4 : 6-*trichlorophenylhydrazone*. When carried out slowly, at intermediate stages m-*nitrobenzaldehyde*-2 : 4-*dichlorophenylhydrazone* and ω-*chloro*-m-*nitrobenzaldehyde*-2 : 4-*dichlorophenylhydrazone* separated from the solution. A smaller quantity of ω-chloro-*m*-nitrobenzaldehyde-*p*-chlorophenylhydrazone was also obtained.

ω-*Chloro*-m-*nitrobenzaldehyde*-2 : 4 : 6-*trichlorophenylhydrazone*, $C_6H_2Cl_3\cdot NH\cdot N{:}CCl\cdot C_6H_4\cdot NO_2$. Chlorine was passed to saturation into a cooled suspension of 5 g. of *m*-nitrobenzaldehydephenylhydrazone in 30 c.c. of chloroform, the dark solution which was first formed finally lightening in colour, and depositing the ω-*chloro*-m-*nitrobenzaldehyde*-2 : 4 : 6-*trichlorophenylhydrazone* as a grey, crystalline mass. This separated from acetic acid, in which it was only moderately soluble, in fine, colourless, hair-like needles, m. p. 157° (yield 5 g.) (Found: Cl, 37·6. $C_{13}H_7O_2N_3Cl_4$ requires Cl, 37·4%).

The same compound separated when chlorine was passed into a suspension of *m*-nitrobenzaldehyde-2 : 4 : 6-trichlorophenylhydrazone in chloroform. A small quantity of the substance, when boiled with an alkaline solution of potassium permanganate, yielded *m*-nitrobenzoic acid, m. p. 140°, thus showing the absence of halogen in the aldehyde nucleus.

Isolation of m-*nitrobenzaldehyde*-2 : 4-*dichlorophenylhydrazone and* ω-*chloro*-m-*nitrobenzaldehyde*-p-*chlorophenylhydrazone*,

$C_6H_3Cl_2\cdot NH\cdot N{:}CH\cdot C_6H_4\cdot NO_2$ and $C_6H_4Cl\cdot NH\cdot N{:}CCl\cdot C_6H_4\cdot NO_2$. Chlorine was cautiously passed into a suspension of *m*-nitrobenzaldehydephenylhydrazone (5 g.) in chloroform (30 c.c.) until the solution formed darkened and set to a solid brown mass, probably containing unstable compounds of the hydrazones with hydrogen chloride. On the addition of an equal volume of alcohol, it changed to a clean yellow, crystalline mass of *m*-nitrobenzaldehyde-2 : 4-dichlorophenylhydrazone, m. p. 211° after recrystallisation from acetic

acid. The chloroform and alcohol mother-liquor slowly deposited crystals containing *ω-chloro*-m-*nitrobenzaldehyde*-p-*chlorophenylhydrazone*. After two recrystallisations from acetic acid this melted at 130°, but since further purification in this way was difficult, it was dissolved in boiling alcohol, a few c.c. of concentrated ammonia solution were added, the solution was acidified with concentrated hydrochloric acid, diluted with hot water, filtered, and made alkaline with ammonia; the *m*-nitrobenzaldehyde-*p*-chlorophenylhydrazidine which separated crystallised from alcohol in deep red needles, m. p. 150°, identical with the hydrazidine obtained from ω-bromo-*m*-nitrobenzaldehyde-*p*-chlorophenylhydrazone (p. 1694).

Isolation of ω-chloro-m-*nitrobenzaldehyde*-2 : 4-*dichlorophenylhydrazone*, $C_6H_3Cl_2\cdot NH\cdot N{:}CCl\cdot C_6H_4\cdot NO_2$. In another experiment, the passage of chlorine was cautiously continued until the brown precipitate containing *m*-nitrobenzaldehyde-2 : 4-dichlorophenylhydrazone (above) just redissolved. The solution on standing, or on the addition of an equal volume of alcohol, yielded pale yellow crystals of *ω-chloro*-m-*nitrobenzaldehyde*-2 : 4-*dichlorophenylhydrazone*. This crystallised from acetic acid, in which it was moderately soluble, in long, pale yellow needles, m. p. 158° (yield 4 g.) (Found : Cl, 31·0. $C_{13}H_8O_2N_3Cl_3$ requires Cl, 30·9%).

The constitution of the compound was confirmed as follows : A mixture of 2 g. of β-*m*-nitrobenzoyl-2 : 4-dichlorophenylhydrazine and 3 g. (2 mols.) of phosphorus pentachloride was maintained for a few minutes at 190°, and the cooled product treated with water and extracted with ether. To the residue after evaporation were added a few c.c. of alcohol; the yellow solid which separated, m. p. 158° after recrystallisation from acetic acid, was identical with the chlorination product described above.

Action of Chlorine upon p-*Nitrobenzaldehydephenylhydrazone.*

ω-Chloro-p-*nitrobenzaldehyde*-2 : 4 : 6-*trichlorophenylhydrazone*. A cooled suspension of 5 g. of *p*-nitrobenzaldehydephenylhydrazone in 100 c.c. of chloroform was saturated with chlorine. The crystalline mass of *ω-chloro*-p-*nitrobenzaldehyde*-2 : 4 : 6-*trichlorophenylhydrazone* obtained separated from acetic acid, in which it was sparingly soluble, in fine, pale yellow needles, m. p. 164° (yield 6 g.) (Found : Cl, 37·5. $C_{13}H_7O_2N_3Cl_4$ requires Cl, 37·4%).

The same compound was obtained by the chlorination under similar conditions of *p*-nitrobenzaldehyde-2 : 4 : 6-trichlorophenylhydrazone.

When boiled with an alkaline solution of potassium permanganate, it yielded *p*-nitrobenzoic acid, m. p. 238°.

Isolation of intermediate products in the chlorination of p-*nitro-*

benzaldehydephenylhydrazone. These products can be obtained with much greater ease than the analogous compounds formed in the chlorination of *m*-nitrobenzaldehydephenylhydrazone, the main products, *ω-chloro*-p-*nitrobenzaldehyde*-p-*chlorophenylhydrazone* and *ω-chloro*-p-*nitrobenzaldehyde*-2 : 4-*dichlorophenylhydrazone*, separating in good quantity at different stages of the reaction.

ω-Chloro-p-*nitrobenzaldehyde*-p-*chlorophenylhydrazone*. Chlorine was cautiously passed into a fine suspension in chloroform (5 g. in 100 c.c.) of *p*-nitrobenzaldehydephenylhydrazone, until the red solution first formed just became brown. Orange crystals of *ω-chloro*-p-*nitrobenzaldehyde*-p-*chlorophenylhydrazone* separated slowly, and a further quantity on addition of alcohol. It crystallised from acetic acid, in which it was moderately soluble, in orange needles, m. p. 213° (yield 3 g.) (Found: Cl, 23·0. $C_{13}H_9O_2N_3Cl_2$ requires Cl, 22·9%). The same compound separated when *p*-nitrobenzaldehyde-*p*-chlorophenylhydrazone was similarly chlorinated. On boiling with alkaline permanganate solution, it yielded *p*-nitrobenzoic acid, m. p. 238°.

ω-Chloro-p-*nitrobenzaldehyde*-2 : 4-*dichlorophenylhydrazone*. The cautious passage of chlorine was continued beyond the stage described above, until the orange crystals of ω-chloro-*p*-nitrobenzaldehyde-*p*-chlorophenylhydrazone just redissolved. The solution almost immediately set to a mass of bright yellow crystals of *ω-chloro*-p-*nitrobenzaldehyde*-2 : 4-*dichlorophenylhydrazone*. This crystallised from acetic acid, in which it was sparingly soluble, in long, bright yellow, hair-like needles, m. p. 199° (yield 6 g.) (Found: Cl, 31·2. $C_{13}H_8O_2N_3Cl_3$ requires Cl, 30·9%).

The same compound separated when *p*-nitrobenzaldehyde-2 : 4-dichlorophenylhydrazone was similarly chlorinated.

Conversion of ω-Chlorohydrazones into α-Acetyl-β-nitrobenzoylphenylhydrazines.—When the ω-chloro-*m*- and -*p*-nitrobenzaldehydechlorophenylhydrazones are boiled for 2 hours with an excess of anhydrous sodium acetate and acetic acid, they are quantitatively converted into the corresponding α-acetyl-β-nitrobenzoylchlorophenylhydrazines, which separate as solids when the acetic acid solutions are poured into water. They are best recrystallised from alcohol, in which the *p*-chloro-derivatives are easily soluble and the di- and tri-chloro-derivatives moderately easily soluble. These α-acetyl-β-nitrobenzoylchlorophenylhydrazines are readily hydrolysed when heated with a mixture of alcohol and hydrochloric acid, yielding ethyl acetate, the corresponding nitrobenzoic acid, and the hydrochloride of the corresponding hydrazine, a procedure which provides the easiest method of determining their constitution, and consequently that of the original ω-chlorohydrazones.

α-*Acetyl*-β-m-*nitrobenzoyl*-2 : 4-*dichlorophenylhydrazine*, $C_6H_3Cl_2{\cdot}NAc{\cdot}NH{\cdot}CO{\cdot}C_6H_4{\cdot}NO_2$, was obtained as described above from ω-chloro-*m*-nitrobenzaldehyde-2 : 4-dichlorophenylhydrazone, and also directly from β-*m*-nitrobenzoyl-2 : 4-dichlorophenylhydrazine by boiling for a few minutes with acetyl chloride. It forms colourless plates, m. p. 155—156° (Found : Cl, 19·3. $C_{15}H_{11}O_4N_3Cl_2$ requires Cl, 19·3%).

The substance (1 g.) was boiled for 3 hours with 50 c.c. of alcohol and 20 c.c. of hydrochloric acid. The crystals of 2 : 4-dichlorophenylhydrazine hydrochloride that separated on cooling were identified by conversion into *o*-nitrobenzaldehyde-2 : 4-dichlorophenylhydrazone, m. p. 192·5°. The mother-liquor was neutralised and alcohol and ethyl acetate were distilled off. On acidifying the residue and cooling, crystals of *m*-nitrobenzoic acid, m. p. 140°, separated.

α-*Acetyl*-β-p-*nitrobenzoyl*-p-*chlorophenylhydrazine*, obtained similarly, forms long prisms with domed ends, m. p. 167° (Found : Cl, 10·7. $C_{15}H_{12}O_4N_3Cl$ requires Cl, 10·6%). When boiled with alcohol and hydrochloric acid it yielded acetic acid, *p*-nitrobenzoic acid, and *p*-chlorophenylhydrazine.

α-*Acetyl*-β-p-*nitrobenzoyl*-2 : 4-*dichlorophenylhydrazine* crystallises in long, colourless, six-sided plates, m. p. 158° (Found : Cl, 19·4. $C_{15}H_{11}O_4N_3Cl_2$ requires Cl, 19·3%). When boiled with a mixture of hydrochloric acid and alcohol it yielded acetic acid, *p*-nitrobenzoic acid, and 2 : 4-dichlorophenylhydrazine.

α-*Acetyl*-β-m-*nitrobenzoyl*-2 : 4 : 6-*trichlorophenylhydrazine* was prepared as described above from ω-chloro-*m*-nitrobenzaldehyde-2 : 4 : 6-trichlorophenylhydrazone, and also directly from β-*m*-nitrobenzoyl-2 : 4 : 6-trichlorophenylhydrazine by boiling for a few minutes with acetyl chloride. It crystallises in small, colourless prisms, m. p. 143° (Found : Cl, 26·3. $C_{15}H_{10}O_4N_3Cl_3$ requires Cl, 26·4%).

Hydrolysis of α-*Acetyl*-β-m-*nitrobenzoyl*-2 : 4 : 6-*trichlorophenylhydrazine to* m-*Nitrobenzoic Acid and* α-*Acetyl*-2 : 4 : 6-*trichlorophenylhydrazine*.—α-Acetyl-β-*m*-nitrobenzoyl-2 : 4 : 6-trichlorophenylhydrazine (4 g.) was boiled for 3 hours with 30 c.c. of alcohol and 20 c.c. of hydrochloric acid. On making alkaline with sodium carbonate and diluting with water, a colourless, oily liquid separated, which was removed. From the aqueous layer, on acidification, *m*-nitrobenzoic acid crystallised. The oily liquid did not crystallise alone or in contact with solvents. To its solution in warm alcohol *m*-nitrobenzaldehyde (2 parts) was added; on cooling, acetyl-*m*-nitrobenzaldehyde-2 : 4 : 6-trichlorophenylhydrazone, $C_6H_2Cl_3{\cdot}NAc{\cdot}N{:}CH{\cdot}C_6H_4{\cdot}NO_2$, separated in colourless, rectangular plates, m. p. 204°, identical with

the substance obtained by the acetylation of *m*-nitrobenzaldehyde-2 : 4 : 6-trichlorophenylhydrazone. The yield was 70%, and the original oily liquid from the hydrolysis must therefore have been mainly α-acetyl-2 : 4 : 6-trichlorophenylhydrazine, $C_6H_2Cl_3 \cdot NAc \cdot NH_2$.

α-Acetyl-β-p-nitrobenzoyl-2 : 4 : 6-trichlorophenylhydrazine was prepared as above from ω-chloro-*p*-nitrobenzaldehyde-2 : 4 : 6-trichlorophenylhydrazone, and also directly by boiling *p*-nitrobenzoyl-2 : 4 : 6-trichlorophenylhydrazine for a few minutes with acetyl chloride. It forms flat, colourless needles, m. p. 121° (decomp.) (Found : Cl, 26·4. $C_{15}H_{10}O_4N_3Cl_3$ requires Cl, 26·5%). When boiled with hydrochloric acid and alcohol, it behaves like the corresponding *m*-nitrobenzoyl derivative, yielding α-acetyl-2 : 4 : 6-trichlorophenylhydrazine as a colourless oil, and *p*-nitrobenzoic acid.

Conversion of ω-Chlorohydrazones into Hydrazidines.—In each case the ω-chloro-compound was boiled with alcohol and a slight excess of concentrated aqueous ammonia until the original solid had completely dissolved. The hydrazidine formed separated either during the reaction or on subsequent cooling. These hydrazidines are strongly coloured compounds which combine with hydrochloric acid (1 mol.) to form colourless salts that crystallise well when solutions of the bases in hot dilute hydrochloric acid are allowed to cool.

m-*Nitrobenzaldehyde*-p-*chlorophenylhydrazidine*,

$$C_6H_4Cl \cdot NH \cdot N{:}C(NH_2) \cdot C_6H_4 \cdot NO_2,$$

is very soluble in alcohol, from which it separates in deep red needles, m. p. 150° (Found : Cl, 12·3. $C_{13}H_{11}O_2N_4Cl$ requires Cl, 12·2%).

m-*Nitrobenzaldehyde*-2 : 4-*dichlorophenylhydrazidine*,

$$C_6H_3Cl_2 \cdot NH \cdot N{:}C(NH_2) \cdot C_6H_4 \cdot NO_2,$$

crystallises from alcohol, in which it is moderately easily soluble, in thin, irregular, orange plates, m. p. 154° (Found : Cl, 21·9. $C_{13}H_{10}O_2N_4Cl_2$ requires Cl, 21·75%). The *hydrochloride* is easily soluble in alcohol, less easily soluble in water. It separates from a mixture of these solvents in clusters of colourless needles, m. p. 220° (decomp.).

m-*Nitrobenzaldehyde*-2 : 4 : 6-*trichlorophenylhydrazidine* is sparingly soluble in alcohol, separating in fine, yellow leaflets, m. p. 194° (Found : Cl, 29·9. $C_{13}H_9O_2N_4Cl_3$ requires Cl, 29·6%). The *hydrochloride* forms colourless plates, m. p. 230° (decomp.), sparingly soluble in water and more soluble in alcohol.

p-*Nitrobenzaldehyde*-2 : 4 : 6-*trichlorophenylhydrazidine* crystallises from alcohol, in which it is moderately easily soluble, in dark red needles, m. p. 157° (Found : Cl, 29·8%). The *hydrochloride*, which is sparingly soluble in water, forms colourless, compact prisms, m. p. 260° (decomp.).

Action of Bromine upon m- *and* p-*Nitrobenzaldehydephenylhydrazones.*—The bromination of the nitrobenzaldehydephenylhydrazones was studied by Ciusa and Vecchiotti (*Gazzetta*, 1916, **46**, i, 240), who obtained the final products and, in the case of the *m*- and *p*-nitrobenzaldehydehydrazones, correctly regarded them as ω-bromonitrobenzaldehyde-2 : 4-dibromophenylhydrazones. They did not isolate the intermediate ω-bromonitrobenzaldehyde-*p*-bromophenylhydrazones.

ω-*Bromo*-m-*nitrobenzaldehyde*-p-*bromophenylhydrazone*,

$$C_6H_4Br\cdot NH\cdot N{:}CBr\cdot C_6H_4\cdot NO_2.$$

To a suspension of 5 g. (1 mol.) of *m*-nitrobenzaldehydephenylhydrazone in 100 c.c. of acetic acid was added a solution of 6 g. of bromine (slightly less than 2 mols.) in acetic acid. As the hydrazone dissolved, a yellow precipitate of the dibromo-compound separated, which crystallised from acetic acid, in which it was moderately easily soluble, in glistening, yellow plates, m. p. 146·5° (yield 6 g.). The use of less bromine caused the separation of the same compound in smaller amount, whilst the use of exactly 2 mols. of bromine led to the formation of small quantities of the tribromo-compound (Found : Br, 40·3. $C_{13}H_9O_2N_3Br_2$ requires Br, 40·1%). The same compound was also obtained by similarly brominating *m*-nitrobenzaldehyde-*p*-bromophenylhydrazone.

ω-*Bromo*-m-*nitrobenzaldehyde*-2 : 4-*dibromophenylhydrazone.* In a second experiment a larger quantity of bromine, 10 g. (3 mols.), was added, the ω-bromo-*m*-nitrobenzaldehyde-2 : 4-dibromophenylhydrazone finally separating as a thick, crystalline mass. It crystallised from acetic acid in bright yellow needles, m. p. 179° (yield 7 g.) (Found : Br, 50·4%). The same compound was obtained by similarly brominating *m*-nitrobenzaldehyde-2 : 4-dibromophenylhydrazone. When boiled with alkaline permanganate solution, it yielded *m*-nitrobenzoic acid, m. p. 140°.

The following ω-bromo-hydrazones were similarly prepared by the addition of bromine (1 mol.) to a suspension of the appropriate *m*-nitrobenzaldehydephenylhydrazone :

ω-*Bromo*-m-*nitrobenzaldehyde*-2 : 4 : 6-*tribromophenylhydrazone* crystallises in long, colourless, hair-like needles, m. p. 173°, sparingly soluble in acetic acid and alcohol (Found : Br, 57·7. $C_{13}H_7O_2N_3Br_4$ requires Br, 57·5%).

ω-*Bromo*-m-*nitrobenzaldehyde*-p-*chlorophenylhydrazone* crystallises from acetic acid, in which it is moderately easily soluble, in bright yellow, rectangular plates, m. p. 133° (Found : Cl + Br, 32·6. $C_{13}H_9O_2N_3ClBr$ requires Cl + Br, 32·6%).

ω-*Bromo*-p-*nitrobenzaldehyde*-p-*bromophenylhydrazone*,

$$C_6H_4Br\cdot NH\cdot N{:}CBr\cdot C_6H_4\cdot NO_2,$$

was prepared by the two methods described in the case of the isomeric *m*-nitro-derivative. It crystallises from acetic acid, in which it is moderately easily soluble, in light orange leaflets, m. p. 224° (Found: Br, 40·0%).

ω-*Bromo*-p-*nitrobenzaldehyde*-2 : 4-*dibromophenylhydrazone* separated when a solution of bromine (10 g.; 3 mols.) was added to a suspension in acetic acid of 5 g. of *p*-nitrobenzaldehydephenylhydrazone (1 mol.), or when bromine (1 mol.) was added to *p*-nitrobenzaldehyde-2 : 4-dibromophenylhydrazone (1 mol.). It crystallises from acetic acid, in which it is sparingly soluble, in long, deep yellow needles, m. p. 214° (Found: Br, 50·2. $C_{13}H_8O_2N_3Br_3$ requires Br, 50·2%). When boiled with alkaline permanganate, the compound yielded *p*-nitrobenzoic acid, m. p. 238°.

By boiling the ω-bromohydrazones with sodium acetate in acetic acid α-acetyl-β-nitrobenzoylbromophenylhydrazines were obtained. These were recrystallised from alcohol, in which the monobromo-derivatives are more easily soluble than the dibromo-derivatives.

α-*Acetyl*-β-m-*nitrobenzoyl*-p-*bromophenylhydrazine*,

$$C_6H_4Br\cdot NAc\cdot NH\cdot CO\cdot C_6H_4\cdot NO_2,$$

was obtained from ω-bromo-*m*-nitrobenzaldehyde-*p*-bromophenylhydrazone as a colourless, amorphous solid which could not be made to crystallise. When boiled in alcohol with hydrochloric acid, it yielded acetic acid, *p*-bromophenylhydrazine, and *m*-nitrobenzoic acid.

α-*Acetyl*-β-m-*nitrobenzoyl*-2 : 4-*dibromophenylhydrazine* was obtained from ω-bromo-*m*-nitrobenzaldehyde-2 : 4-dibromophenylhydrazone, and also from β-*m*-nitrobenzoyl-2 : 4-dibromophenylhydrazine, by boiling with acetyl chloride. It forms colourless, compact prisms, m. p. 169° (Found: Br, 35·1. $C_{15}H_{11}O_4N_3Br_2$ requires Br, 35·0%). When boiled with alcohol and hydrochloric acid, it yielded acetic acid, 2 : 4-dibromophenylhydrazine, and *m*-nitrobenzoic acid.

α-*Acetyl*-β-m-*nitrobenzoyl*-2 : 4 : 6-*tribromophenylhydrazine* crystallises from acetic acid, in which it is moderately easily soluble, in fine, colourless prisms, m. p. 180° (Found: Br, 44·7. $C_{15}H_{10}O_4N_3Br_3$ requires Br, 44·8%). On boiling for 3 hours with hydrochloric acid and alcohol, it yielded *m*-nitrobenzoic acid and a colourless, oily liquid. This formed a crystalline hydrazone (m. p. 230°) with *m*-nitrobenzaldehyde, identical with acetyl-*m*-nitrobenzaldehyde-2 : 4 : 6-tribromophenylhydrazone,

$$C_6H_2Br_3\cdot NAc\cdot N{:}CH\cdot C_6H_4\cdot NO_2,$$

obtained by the acetylation of *m*-nitrobenzaldehyde-2 : 4 : 6-tribromophenylhydrazone. The original oily liquid must therefore have been α-acetyl-2 : 4 : 6-tribromophenylhydrazine.

α-*Acetyl*-β-p-*nitrobenzoyl*-p-*bromophenylhydrazine* crystallises in colourless prisms, m. p. 169—170° (Found : Br, 21·25. $C_{15}H_{12}O_4N_3Br$ requires Br, 21·2%). When boiled with alcohol and hydrochloric acid, it yielded acetic acid, *p*-nitrobenzoic acid, and *p*-bromophenylhydrazine.

α-*Acetyl*-β-p-*nitrobenzoyl*-2 : 4-*dibromophenylhydrazine* forms stout, colourless octahedral crystals, m. p. 201—202° (Found : Br, 35·2. $C_{15}H_{11}O_4N_3Br_2$ requires Br, 35·0%). When boiled with hydrochloric acid and alcohol, it yielded acetic acid, *p*-nitrobenzoic acid, and 2 : 4-dibromophenylhydrazine. The same compound was prepared by boiling β-*p*-nitrobenzoyl-2 : 4-dibromophenylhydrazine with acetyl chloride for a few minutes.

The following hydrazidines were prepared from the corresponding ω-bromohydrazones by warming them with alcoholic ammonia.

m-*Nitrobenzaldehyde*-p-*bromophenylhydrazidine*,

$$C_6H_4Br\cdot NH\cdot N{:}C(NH_2)\cdot C_6H_4\cdot NO_2,$$

separates from alcohol, in which it is moderately easily soluble, in fine, dark red plates, m. p. 145° (decomp.). The *hydrochloride* crystallises in colourless plates, m. p. 200° (decomp.).

m-*Nitrobenzaldehyde*-2 : 4-*dibromophenylhydrazidine* separates from alcohol, in which it is very sparingly soluble, in small, dark red plates, m. p. 182° (decomp.) (Found : Br, 38·8. $C_{13}H_{10}O_2N_4Br_2$ requires Br, 38·6%). The *hydrochloride* forms colourless leaflets, m. p. 225° (decomp.).

p-*Nitrobenzaldehyde*-p-*bromophenylhydrazidine* crystallises from alcohol, in which it is moderately easily soluble, in almost black needles, m. p. 155° (decomp.) (Found : Br, 24·0. $C_{13}H_{11}O_2N_4Br$ requires Br, 23·9%). Its *hydrochloride* crystallises in colourless plates, m. p. 210° (decomp.).

p-*Nitrobenzaldehyde*-2 : 4-*dibromophenylhydrazidine* crystallises from alcohol, in which it is moderately easily soluble, in dark bronze-red needles, m. p. 175° (Found : Br, 38·7. $C_{13}H_{10}O_2N_4Br_2$ requires Br, 38·6%). The *hydrochloride* forms colourless, compact, rhombic plates, m. p. 200° (decomp.).

The following is a brief description of the hydrazones and hydrazines employed in confirming the structure of the α-acetylphenylhydrazines :

Acetyl-m-*nitrobenzaldehyde*-2 : 4 : 6-*trichlorophenylhydrazone*, prepared by boiling *m*-nitrobenzaldehyde-2 : 4 : 6-trichlorophenylhydrazone for a short time with acetic anhydride, separates from alcohol, in which it is moderately easily soluble, in colourless, rectangular plates, m. p. 204° (Found : Cl, 27·4. $C_{15}H_{10}O_3N_3Cl_3$ requires Cl, 27·5%).

Acetyl-m-*nitrobenzaldehyde*-2 : 4 : 6-*tribromophenylhydrazone*, pre-

pared in a similar manner, crystallises from acetic acid, in which it is moderately easily soluble, in thick, colourless tablets, m. p. 230° (Found: Br, 46·0. $C_{15}H_{10}O_3N_3Br_3$ requires Br, 46·1%).

The following nitrobenzoylphenylhydrazines, prepared directly by the Schotten-Baumann method, were all crystallised from alcohol, in which they are moderately easily soluble.

β-m-*Nitrobenzoyl*-2 : 4 : 6-*trichlorophenylhydrazine*; long, six-sided needles, m. p. 205° (Found: Cl, 29·6. $C_{13}H_8O_3N_3Cl_3$ requires Cl, 29·5%).

β-p-*Nitrobenzoyl*-2 : 4 : 6-*trichlorophenylhydrazine*; stout, colourless plates, m. p. 203° (Found: Cl, 29·7. $C_{13}H_8O_3N_3Cl_3$ requires Cl, 29·5%).

β-m-*Nitrobenzoyl*-2 : 4-*dichlorophenylhydrazine*; elongated, colourless plates, m. p. 196°.

β-m-*Nitrobenzoyl*-2 : 4-*dibromophenylhydrazine*; colourless needles, m. p. 210° (Found: Br, 38·8. $C_{13}H_9O_3N_3Br_2$ requires Br, 38·5%).

β-p-*Nitrobenzoyl*-2 : 4-*dibromophenylhydrazine*; pale yellow needles, m. p. 227°.

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CCXXVII.—*The Tautomerism of Dyads. Part IV. New Evidence of the Tautomeric Mobility of Oximes.*

By JOHN PREEDY GRIFFITHS and CHRISTOPHER KELK INGOLD.

THE purpose of this paper is to place dyad migration in oximes on a secure experimental basis such as has been provided in the cases of hydrogen cyanide, acetylene, and some monosubstitution products of the latter (E. H. Ingold, J., 1922, **121**, 1604; 1924, **125**, 1528; this vol., p. 1199), and to emphasise the suggestion, already made or foreshadowed by others (notably Brady and Dunn, J., 1916, **109**, 659; 1924, **125**, 291) that tautomerism of the dyad type, superimposed on the stereochemical theory of Hantzsch and Werner, constitutes the explanation of the isomerism and reactions of oximes.

$$[H]C{:}N \rightleftharpoons C{:}NH \qquad [H]C{:}\overset{|}{C} \rightleftharpoons C{:}\overset{|}{C}[H]$$

$$\text{(I.)}\quad [H]\overset{||}{N}{:}O \rightleftharpoons \overset{||}{N}{\cdot}O[H]\quad \text{(II.)} \qquad \ldots \qquad \text{(A)}$$

Whilst the retention of Hantzsch and Werner's stereochemical hypothesis is, for strong reasons, necessary to explain the isomerism of the oximes themselves, a structural addition to the theory is

just as imperatively required to account for their ethers (*Ann. Report*, 1924, p. 111).

(III.) $\begin{matrix} R\cdot C\cdot R' \\ \| \\ Alk\cdot N\cdot O \end{matrix}$ (*N*-Ethers: *syn*- and *anti*-forms.)

$\begin{matrix} R\cdot C\cdot R' \\ \| \\ N\cdot OAlk. \end{matrix}$ (IV.) (*O*-Ethers: *syn*- and *anti*-forms.)

Formula (IV) for the *O*-ethers has long been generally approved, and, in view of evidence recently accumulated,* and of analogy with azoxy- and aliphatic diazo-compounds, no apology is necessary for using the "nitrone" formula (III), rather than the older *iso*oxime formula $\begin{matrix} RR'C\text{—}NAlk \\ \diagdown O \diagup \end{matrix}$, for the *N*-ethers.†

The study of tautomerism in numerous other cases has shown that the isolation of isomeric alkyl derivatives may be taken as an indication of the possibility of tautomeric interchange between parent hydrogen compounds of corresponding constitution. If, therefore, the structures given to the oxime-ethers (III) and (IV) be accepted, a *prima facie* case in favour of tautomerism of the dyad type between corresponding parent forms (I and II) is established (equation A).‡

Physical methods, which have the advantage of avoiding all the unknown disturbances attending the use of a chemical reagent, were applied to the problem; but, probably owing to the mobility of the oxime system, success was not achieved. Another method

* Thus towards diphenylketen, an almost universal reagent for double linkings, both the double bonds act separately (Staudinger and Miescher, *Helv. Chim. Acta*, 1919, **2**, 554):

$$>C{:}N{:}O \longrightarrow >C{:}N\begin{matrix}\diagup CPh_2 \\ \diagdown CO \\ \quad O\end{matrix} \longrightarrow CPh_2\begin{matrix}\diagup CO \\ \diagdown N \\ >C \quad O\end{matrix}\begin{matrix}\diagup CPh_2 \\ \diagdown CO. \\ \quad O\end{matrix}$$

Many other examples might be given. Sugden's work (this vol., p. 1177) supplies strong confirmation from the physical side.

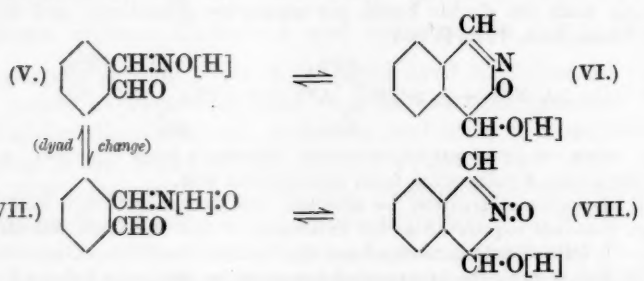
† If the nitrone structure be adopted, the existence of *syn*- and *anti*-*N*-ethers does not require an *ad hoc* extension of the Hantzsch-Werner hypothesis: it follows automatically from the optical resolution of amine-oxides, $R_1R_2R_3N{:}O$, just as the geometrical isomerism of ethylenes follows from the optical activity of methanes of the type $R_1R_2R_3R_4C$.

‡ It is not intended to preclude the intervention of the ring-form $\begin{matrix} >C\text{—}NR \\ \diagdown O \diagup \end{matrix}$ in certain decompositions, and, as an intermediate, in a few methods of formation of *N*-ethers and of oximes. Similarly, one cannot dismiss the nitroso-isomeride $>CH\cdot N{:}O$, which often constitutes an intermediate stage in reactions leading to oximes. All the available evidence shows, however, that these structures represent comparatively unstable oxime-forms, and may be looked upon as constituting minor ramifications of the tautomeric system, the main reversible reaction in which is, as will be shown, that represented by equation A.

of investigation was therefore sought, which, whilst still avoiding, so far as possible, the complications arising from the use of reagents, would clearly and certainly distinguish between the two expected forms and detect any equilibrium between them.

The object in view was ultimately attained by utilising the special properties of phthalaldehydemonoxime. This substance, ordinarily represented by (V), contains all the essential features which give ring-chain tautomeric character to a sugar, the residues –CH:O and –OH being present in such relative positions that they can interact with the formation of an "oxide" ring and a "glucoside-yielding" hydroxyl group. If, therefore, the structure –CH:NOH, present in (V), be really one of the tautomeric forms of the oxime group, we should expect, just as in the case of a sugar, to be able to crystallise the cyclic tautomeric form (VI). This individual, moreover, although a tautomeric substance, should be sufficiently well differentiated chemically from any other possible isomeride as to leave no doubt about its constitution, and therefore none about the particular oxime structure from which it is derived.

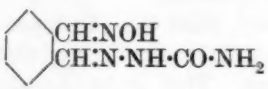
On the other hand, if an isomeride of the constitution (VII) should also be present in any considerable quantity, the fact should be rendered evident by the tendency, possessed by this individual also, to pass into, and crystallise in the form of, its ring tautomeride (VIII). This structure, based on the *iso*indole ring system, also is strikingly differentiated from any other possible isomeride:



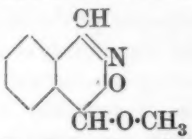
Thus the chemical differences to be expected from the simple dyad change (V) $\rightleftharpoons$ (VII) become magnified by the production, through ring closure, of the more distinctive structures (VI) and (VIII). At the same time, the mobile dyad equilibrium becomes partly "set" through association with the slower ring-chain changes. These are just the conditions which are required to render the dyad change open to experimental confirmation.

All these theoretical anticipations have been realised experimentally.

The ring form (VI), which was isolated in the crystalline condition, exhibited clear evidence of its constitution and of its structural analogy with the reducing sugars; it showed the usual aldehydic reactions (of the open-chain form V), yielding, for instance, the *semicarbazone* (IX), and also united readily with methyl alcohol, giving a *methyl* derivative *devoid of aldehydic properties*. This must therefore be derived from (VI) by the replacement of the bracketed hydrogen atom, and all its reactions, for instance, the ease with which it is hydrolysed back to the parent substance by a small quantity of mineral acid, emphasise its resemblance to a glucoside and leave no doubt as to the correctness of formula (X).



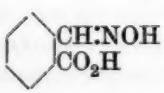
(IX; derivative of V.)



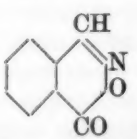
(X; derivative of VI.)

It is clear, therefore, that in solutions of the substance under discussion we have the ring-chain tautomeric system (V) $\rightleftharpoons$ (VI).

A closer study proved, moreover, that the principal phase in solution, as well as the solid substance itself, is represented by the ring-formula (VI). Thus, in contrast to the completeness and rapidity with which the "glucosidic" methyl derivative (X) is formed from freshly-prepared solutions of the parent, the aldehydic reactions of the latter, *e.g.*, the formation of the semicarbazone (IX), are noticeably sluggish: a solution of (VI), treated after some time with semicarbazide acetate, deposits a small quantity of the semicarbazone, but the complete precipitation of this substance requires a considerable period; and if a freshly-prepared solution of (VI) is used, no initial deposition is observed. It is noteworthy also that, although the main product of the oxidation of (VI) by cold neutral permanganate is *o*-carboxybenzaldoxime anhydride (XII), evidently derived directly from the ring compound, a small amount of the oxime-acid (XI), the normal product of oxidation of (V), is formed simultaneously. Observations of this kind make it quite evident that, as with sugars, the ring phase is the more stable one.



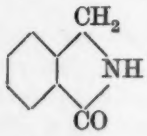
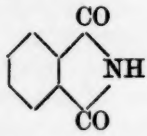
(XI; by-product.)



(XII; main product.)

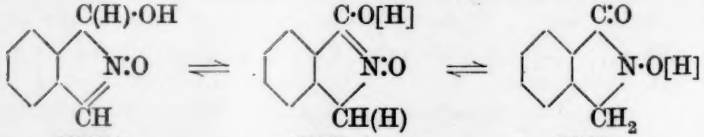
Evidence of the existence of a second oxime structure (VII) was obtained by the isolation of a second ring-compound (VIII), which

resembled the first in certain respects (for instance, in the absence from its methylation product of all aldehydic properties), but differed markedly from it in others. The key to its constitution was found in the fact that on reduction it gave phthalimidine (XIII), thus revealing the presence of the heterocyclic nucleus on which the anticipated formula (VIII) is based.

(XIII.)   (XIV.)

On oxidation phthalimide (XIV) was obtained.

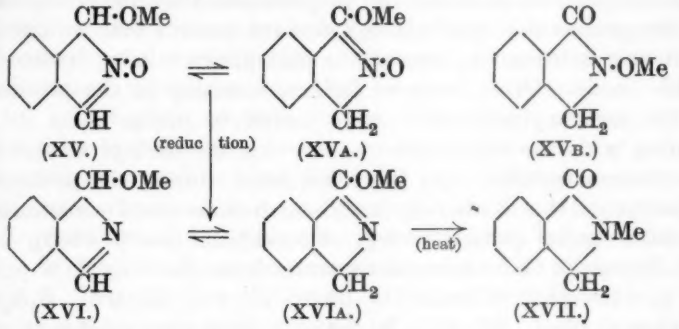
Closer examination showed, however, that the substance is not adequately represented by formula (VIII) alone, but that it is capable of reacting in several forms. This is to be expected. Obviously a substance of formula (VIII) would be susceptible to the type of triad change which is apparently common to all compounds containing an unsaturated five-membered ring fused to the benzene nucleus, as in indene, benzimineazole, and aziminobenzene (Ingold and Piggott, J., 1922, **121**, 2381). The second individual involved in this kind of tautomeric interchange would have formula (VIIIA). This, however, contains a system of the type known to undergo the "tetrad" change into an *N*-hydroxy-isomeride (Bamberger, *Annalen*, 1920, **420**, 137), and it should therefore pass reversibly into an individual of the formula (VIIIB).



(VIII.) (VIIIA.) (VIIIB.)

There is experimental evidence favouring all these formulæ. First, whilst any of the three forms might yield phthalimidine on reduction, only (VIII) can adequately account for aldehydic reactions depending on the opening of the heterocyclic ring. In addition, however, the compound forms a yellow sodium salt and an intensely coloured iron salt; and (VIII) cannot account for this, although either of (VIIIA) and (VIIIB) can do so. Finally, the compound forms two isomeric *methyl* derivatives. One of these, the main product, is obviously an *N*-methoxy-compound, derived from (VIIIB), for, unlike its isomeride, it cannot be reduced to a phthalimidine without previous hydrolysis; this methyl derivative is therefore represented by formula (XVB). The second methyl derivative (by-product) is a *C*-methoxy-compound, derived from

either (VIII) or (VIIIA), as is proved by the fact that it yields *O-methylphthalimidine* (XVI or XVIA) on reduction; the by-product must therefore be represented either by (XV) or by (XVA), or, more probably, by both.



O-Methylphthalimidine readily passes into *N*-methylphthalimidine (XVII), a type of isomeric change which is not uncommon and has for long been exemplified by the transformation of cyanuric into *iso*cyanuric esters on heating.

Further details with regard to the cyclic and aldehydic reactions of the compounds (VI) and (VIII), and the conditions of their interconversion, will be found in the experimental portion of this paper; but the summary already given will be sufficient indication as to the manner in which the isolation and study of these compounds establishes the fundamental dyad change of the oxime group.

EXPERIMENTAL.

Phthalaldehyde was prepared by hydrolysing with aqueous alcoholic potassium oxalate the ωωω′ω′-tetrabromoxylene obtained by brominating boiling *o*-xylene (Thiele and Gunther, *Annalen*, 1906, **347**, 107).

1-*Hydroxy*-2 : 3-*benzoxazine* (VI).—Phthalaldehyde (13·4 g.), dissolved in 30 c.c. of methyl alcohol, was gradually mixed in the cold with an aqueous solution (200 c.c.) of hydroxylamine prepared from 6·9 g. of hydroxylamine hydrochloride and 5·4 g. of anhydrous sodium carbonate. After a few minutes, the solution was extracted with much ether, and the extract washed with water, dried with calcium chloride by shaking, concentrated, and seeded with a crystal of hydroxybenzoxazine obtained from a previous experiment, when the substance crystallised (70% yield). A further quantity could be obtained from the ethereal mother-liquor, which also contained, however, some of the isomeric hydroxy*iso*indole oxide. Extraction of the aqueous mother-liquor with ethyl acetate yielded

a further quantity of the latter substance. If, however, at any stage of these extractions the aqueous solution was set aside for a time, the unextracted material became converted into the methoxybenzoxazine described below.

On one or two occasions the preparation of hydroxybenzoxazine by the process described above failed for reasons that we have not been able to discover, almost the sole product being hydroxy*iso*indole oxide. Other cases of failure, resulting in the production of the methoxy-compound, were traced to undue delay in proceeding with the extraction or removing the methyl alcohol from the ethereal extract. On the other hand, during the preliminary experiments the desired hydroxybenzoxazine could sometimes be produced under quite a variety of conditions (see p. 1705).

1-*Hydroxy*-2 : 3-*benzoxazine* separates from ether–ligroin in prisms, m. p. 114—115° (Found: C, 64·5; H, 4·7; N, 9·5. $C_8H_7O_2N$ requires C, 64·4; H, 4·7; N, 9·4%). It is very soluble in ethyl acetate, easily soluble in chloroform or ether, but almost insoluble in ligroin. It reduces Fehling's solution. Its action towards methyl and ethyl alcohols, oxidising agents, and other ketone reagents is described below. Attempts were made to reduce it both in acid and in alkaline solution under various conditions, including those described on pp. 1706–7, but without success, deeply coloured, amorphous products being obtained which could not be purified. No phthalimidine was obtained.

1-*Methoxy*-2 : 3-*benzoxazine* (X).—This may be obtained (*a*) by leaving phthalaldehyde in contact with hydroxylamine (1 mol.) in 30% methyl alcohol, when the compound crystallises; (*b*) from hydroxybenzoxazine by boiling with methyl alcohol, preferably in the presence of a trace of hydrochloric acid; (*c*) from hydroxy*iso*indole oxide by digesting for several days with faintly acidified aqueous methyl alcohol, and then diluting. It separates from ether in glistening plates, m. p. 77° (Found: C, 66·3; H, 5·6; N, 8·7. $C_9H_9O_2N$ requires C, 66·3; H, 5·5; N, 8·6%). It is hydrolysed with great ease with dilute hydrochloric acid, giving hydroxybenzoxazine.

1-*Ethoxy*-2 : 3-*benzoxazine* was prepared like the methoxy-compound, ethyl alcohol being used in place of methyl alcohol. It was obtained crystalline, but, as it tended to separate as an oil from all solvents in which it was not extremely soluble, it was not purified for analysis.

Phthalaldehyde-1-*oxime*-2-*semicarbazone* (IX).—The formation of this substance from hydroxybenzoxazine was studied in some detail and the main results have already been described (p. 1701). The semicarbazone itself can be purified in small quantities by rapid

crystallisation from ethyl acetate, from which a microcrystalline powder separates, m. p. 235° (decomp.) (Found: C, 52·7; H, 5·0. $C_9H_{10}O_2N_4$ requires C, 52·4; H, 4·9%).

Phthalaldehyde-1-*oxime*-2-p-*nitrophenylhydrazone*, prepared from hydroxybenzoxazine like the corresponding semicarbazone, and also from hydroxy*iso*indole oxide by digesting with *p*-nitrophenylhydrazine in acetic acid solution, separated from ethyl acetate in small, yellow prisms, m. p. 175° (decomp.) (Found: C, 59·0; H, 4·4. $C_{14}H_{12}O_3N_4$ requires C, 59·2; H, 4·2%).

Oxidation of 1-*Hydroxy*-2 : 3-*benzoxazine: Formation of* o-*Carboxybenzaldoxime and its Anhydride* (XI and XII).—The hydroxybenzoxazine, dissolved in pure ether, was shaken with successive small quantities of 1% potassium permanganate solution (in all, equiv. to 1 atom of oxygen) containing an excess of magnesium sulphate, the mixture was filtered, extracted with ether, and the aqueous solution acidified and again extracted. *o*-Carboxybenzaldoxime anhydride was recovered from the first extract and was identified by its m. p. (186°) and by its conversion into phthalimide on heating. The small amount of *o*-carboxybenzaldoxime obtained from the second extract was identified by its m. p. (120°) and by converting it into the anhydride.

1(*or* 3)-*Hydroxyisoindole*-2-*oxide* (N-*Hydroxyphthalimidine*) (VIII, etc.).—It is difficult to give precise directions for the preparation of this substance, for not only was it frequently obtained as almost the sole product on repeating as exactly as possible an experiment which had previously yielded hydroxybenzoxazine, but, on other occasions, attempts to repeat a successful preparation of hydroxy*iso*indole oxide gave hydroxybenzoxazine instead. It is believed that accidental seeding is, at any rate partly, responsible for these erratic results. Two circumstances, however, appear definitely to increase the chances of producing hydroxy*iso*indole oxide, namely, (*a*) the presence of alkalis, (*b*) a high temperature. Condition (*a*) can readily be understood, since hydroxy*iso*indole oxide yields a rather stable sodium salt, the formation of which would disturb any equilibrium involving hydroxy*iso*indole oxide, in such a way as to favour the ultimate isolation of this substance at the expense of hydroxybenzoxazine. Condition (*b*) is explicable if, in the dyad equilibrium between (V) and (VII) (p. 1700), a rise of temperature favours the (usually) less permanent form (namely, VII) just as in the cases of hydrogen cyanide and acetylene. The following typical experiments illustrate the employment of these two methods.

(i) The procedure leading to the formation of hydroxybenzoxazine (p. 1703) was repeated, excepting that 6·5 g. of anhydrous sodium

carbonate were employed instead of 5·4 g., the solution being neutralised before the extraction, which was carried out with chloroform in place of ether.

(ii) The procedure detailed on p. 1703 was followed with the exception that all solutions were previously heated at 60°, and mixed at this temperature. The extraction was carried out with ethyl acetate instead of ether, the extract being washed with water and roughly dried by sodium sulphate before evaporation.

The same substance can also be prepared by allowing hydroxybenzoxazine to remain dissolved in solvents (other than alcohols or ketones), or by digesting it with dilute aqueous sodium carbonate and acidifying. 1-Hydroxy*iso*indole-2-oxide separates from chloroform in well-defined prisms, m. p. 181° (Found: C, 64·3; H, 4·8; N, 9·4. $C_8H_7O_2N$ requires C, 64·4; H, 4·7; N, 9·4%). It is readily soluble in chloroform or ethyl acetate, sparingly soluble in ether, and nearly insoluble in water or ligroin. It is soluble in dilute mineral acids, giving colourless solutions, and it is also dissolved by aqueous sodium carbonate (or sodium hydroxide), giving a yellow solution containing a sodium salt, which is precipitated as a yellow powder when an ethyl acetate solution of the hydroxy-compound is mixed with ethereal-alcoholic sodium ethoxide. Ferric chloride gives an intense violet colour, the reaction constituting a delicate test for the substance in dilute solution. It also readily reduces Fehling's solution on warming, and, on digesting with an acetic acid solution of *p*-nitrophenylhydrazine acetate, gives the hydrazone above mentioned. Its action towards oxidising and reducing agents and its behaviour on methylation are described below.

Reduction of 1-*Hydroxyisoindole*-2-*oxide to Phthalimidine* (XIII).—(i) The substance (1 g.), dissolved in 3 c.c. of methyl alcohol, was treated gradually at 50—60° with 32 g. of 3% sodium amalgam, the solution being kept only faintly alkaline by successive additions of glacial acetic acid. After removal of the mercurial layer, the liquid was evaporated to dryness in a vacuum, and the solid residue extracted with warm ethyl acetate, from which crystals of nearly pure phthalimidine separated (m. p. 145—149°). On crystallisation from benzene, it had the correct m. p. (150—151°), and it was then definitely identified by analysis (Found: C, 71·9; H, 5·5. Calc., C, 72·2; H, 5·5%), and by conversion into its nitroso-derivative (m. p. 156°).

(ii) The hydroxy*iso*indole oxide was dissolved in dilute acetic acid and treated with an excess of zinc dust, added sufficiently rapidly to bring the solution to its boiling point towards the end of the process. An excess of ammonia was then added and the

solution extracted with ether, when an almost quantitative yield of phthalimidine was obtained.

(iii) Hydroxy*iso*indole oxide was dissolved in dilute acetic acid and treated with sodium amalgam in the cold, glacial acetic acid being added as required to keep the solution acid. The mercury was separated, an excess of sodium hydroxide added, and the phthalimidine extracted with ether (yield nearly quantitative).

Oxidation of 1-*Hydroxy*iso*indole*-2-*oxide to Benzaldoxime*-o-*carboxylic Acid* (XI) *and Phthalimide.*—This oxidation was carried out like that described on p. 1705 excepting that ethyl alcohol was used in place of ether and that no magnesium sulphate was added. No product was obtained on extracting the filtered solution with ether, but on acidifying and again extracting, a mixture of phthalimide and benzaldoxime-*o*-carboxylic acid was obtained, from which the former was readily separated owing to its smaller solubility in water.

N-*Methoxyphthalimidine* (IXB).—The hydroxy*iso*indole oxide was dissolved in methyl alcohol and treated with the theoretical quantity of methyl-alcoholic sodium methoxide, and then with twice the theoretical amount of methyl iodide. After heating on the water-bath for ½ hour, the excess of methyl iodide and the methyl alcohol were evaporated and the residue was mixed with water and extracted with ether, from which, on evaporation, long needles were obtained, m. p. 74° after crystallisation from ether–ligroin (a mixture with the isomeric methoxy-compound of m. p. 77° melted at 45°) (Found: C, 66·1; H, 5·6. $C_9H_9O_2N$ requires C, 66·3; H, 5·5%). The substance is readily soluble in benzene, ethyl acetate, chloroform, or ether, moderately soluble in ligroin, and insoluble in water. It does not dissolve in alkalis, gives no colour with ferric chloride, does not reduce Fehling's solution, and gives no condensation products with semicarbazide or the arylhydrazines.

Reduction of N-*Methoxyphthalimidine to Phthalimidine.*—Attempts to reduce this substance in neutral solution with zinc dust, ammonium chloride and aqueous methyl alcohol, or in water or dilute acetic acid with sodium amalgam, resulted in the recovery of unchanged material. Reduction took place, however, with tin and hydrochloric acid, and, on pouring the solution into an excess of alkali and extracting with ether, phthalimidine was obtained.

Oxidation of N-*Methoxyphthalimidine to Hydroxy*iso*indole Oxide and Phthalimide.*—The oxidation was carried out in neutral solution by permanganate in presence of magnesium sulphate as described on p. 1705, excepting that sufficient permanganate solution was used to supply three atoms of oxygen. On extraction with ether, a mixture of hydroxy*iso*indole oxide and phthalimide was obtained,

which were separated from each other by fractional crystallisation from ethyl acetate and identified by direct comparison with authentic specimens.

1(*or* 3)-*Methoxy*isoindole-2-*oxide* (IX or IXA) was obtained from the ultimate ether and ether–ligroin residues obtained in the methylation experiment described on p. 1707. The residues from several such experiments were evaporated and then extracted repeatedly with hot ligroin (b. p. 60—70°). On cooling in a freezing mixture, small prisms separated, m. p. 52—53° after softening at 48°, and from the oily residue obtained by evaporation of the ligroin a further quantity of the same substance was isolated by seeding (Found: C, 66·0; H, 5·7. $C_9H_9O_2N$ requires C, 66·3; H, 5·5%). It is readily soluble in all organic solvents, even ligroin, but insoluble in water. It is also insoluble in sodium carbonate solution, but readily soluble in dilute acids. It does not give a colour with ferric chloride, does not reduce Fehling's solution, and gives no condensation products with semicarbazide or the aryl-hydrazines.

*Reduction of Methoxy*isoindole-2-*oxide to* o-*Methylphthalimidine* (XV or XVA).—The substance was treated with successive quantities of zinc dust in a boiling aqueous methyl-alcoholic solution of ammonium chloride, and the filtered solution was evaporated to remove methyl alcohol and extracted with ether. The residue from the ether yielded crystals, which, after draining, melted at about 40°, but owing to their tendency to liquefy under all solvents in which they were not extremely soluble, they were not recrystallised (Found: C, 73·0; H, 6·4. C_9H_9ON requires C, 73·4; H, 6·1%). The constitution of the substance was established by the observations (i) that, on boiling with concentrated hydrochloric acid, it yields phthalimidine, (ii) that, on heating in an open tube until visible decomposition commences, *N*-methylphthalimidine (XVI) is produced. The latter substance was isolated by crystallisation from ether and identified by direct comparison with a specimen prepared by the reduction of *N*-methylphthalimide.

*Oxidation of Methoxy*isoindole-2-*oxide to Phthalimide.*—This oxidation was carried out like that described on p. 1705, using, however, sufficient permanganate to supply rather more than four atoms of oxygen. On working up the product, phthalimide was obtained and identified in the usual way.

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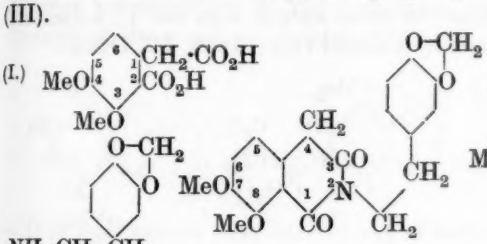
CCXXVIII.—*Synthetical Experiments in the* iso-*Quinoline Group. Part V. Synthesis of Substances allied to Oxyberberine.*

By ROBERT DOWNS HAWORTH, WILLIAM HENRY PERKIN, jun., and HERBERT SHEPPARD PINK.

DURING the course of these synthetical experiments in the group of the berberine alkaloids, it was thought probable that 3 : 4-dimethoxyhomophthalic acid (I) would condense with homopiperonylamine (Ia) with the formation of *2-homopiperonyl-7 : 8-dimethoxyhomophthalimide* (II) and that this substance, under the influence of a suitable dehydrating agent, might yield oxyberberine (III).

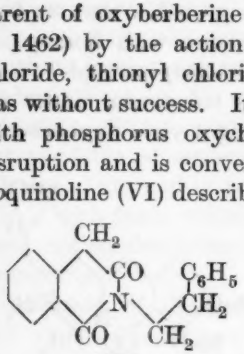


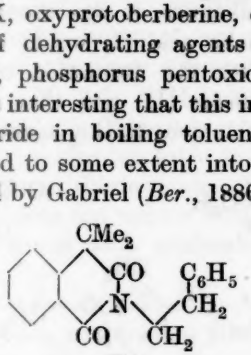
This plan is independent of, but on similar lines to, the successful synthesis of oxyberberine by Perkin, Ray, and Robinson (this vol., p. 740) and as we have now succeeded with its aid in preparing several substances allied to oxyberberine, there can be little doubt that, when it is extended, it will ultimately lead to the synthesis not only of oxyberberine but also of oxypalmatine and allied substances and therefore indirectly to the synthesis of the corresponding alkaloids. The 3 : 4-dimethoxyhomophthalic acid required for the suggested synthesis was unknown and, while we were working out a method for its preparation, we decided to carry out a preliminary investigation with homophthalic acid itself and with 4 : 5-dimethoxyhomophthalic acid, both of which were available.

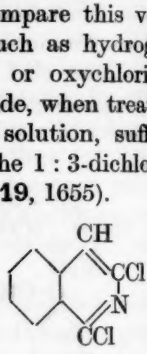
Homophthalic acid may be made from phthalide and potassium cyanide (Wislicenus, *Annalen*, 1886, **233**, 102), a method which, owing to the difficulty in controlling the temperature of interaction, can only be used on a small scale. It may also be prepared by the action of phosphorus pentachloride on 2-*iso*nitroso-1-hydrindone, as described by Perkin and Robinson (J., 1907, **91**, 1073), but the best method is that recommended by Ingold and Piggott (J., 1923, **123**, 1483), namely, from 1-hydrindone by oxidation.

Homophthalic acid condenses readily with β-phenylethylamine

to give 2-β-*phenylethylhomophthalimide* (IV), which dissolves in alkali to a yellow solution with a green fluorescence and condenses with aldehydes at the $-CH_2 \cdot CO-$ group. When treated with methyl iodide and sodium hydroxide, it yields the 4 : 4-*dimethyl* derivative (V) and all attempts to obtain the monomethyl derivative, which would have been useful in the synthesis of substances of the coryd-aline type, were unfortunately unsuccessful. A series of experiments, made with the object of converting this imide into the parent of oxyberberine (X, oxyprotoberberine, compare this vol., p. 1462) by the action of dehydrating agents such as hydrogen chloride, thionyl chloride, phosphorus pentoxide or oxychloride, was without success. It is interesting that this imide, when treated with phosphorus oxychloride in boiling toluene solution, suffers disruption and is converted to some extent into the 1 : 3-dichloro-*iso*quinoline (VI) described by Gabriel (*Ber.*, 1886, **19**, 1655).


(IV.)

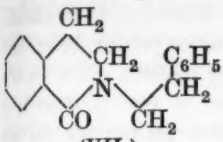

(V.)

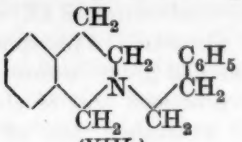

(VI.)

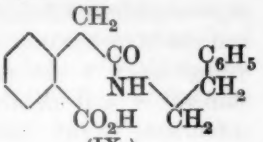
The stability of the imide (IV) to dehydrating agents is probably due to the carbonyl group in the 1-position in the *iso*quinoline ring, and attempts were made to reduce this group without reducing the carbonyl group in the 3-position. It was found that zinc dust and sodium amalgam have no action on alkaline solutions of the imide under mild conditions and that, under vigorous conditions, it slowly undergoes hydrolysis. The imide may, however, be reduced electrolytically to a mixture of 2-β-*phenylethyl*-3 : 4-*dihydro*-1-iso*quinolone* (VII) and 2-β-*phenylethyl*-1 : 2 : 3 : 4-*tetrahydro*iso-*quinoline* (VIII). The former is insoluble in alkali, does not condense with aldehydes or suffer internal condensation when it is treated with phosphorus oxychloride, and cannot therefore be the isomeric 3-*iso*quinolone. It is clearly the carbonyl group in the 3-position in the imide which is the more readily reducible and, so far, it has not been found possible to leave this intact and reduce the group in the 1-position. Experiments are, however, in progress with the object of preparing the 3-keto-derivative synthetically.

When the imide (IV) is heated for several hours with sodium hydroxide, the yellow colour gradually disappears and an N-β-*phenylethylhomophthalamic acid* is produced which probably has structure (IX), but direct evidence of this view of its constitution is not yet available (compare, however, Gabriel and Posner, *Ber.*, 1894, **27**, 2504).

Further experiments on this point are in progress.

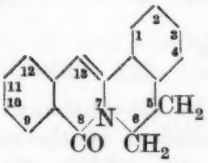

(VII.)

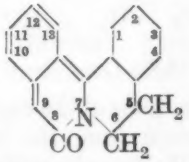

(VIII.)


(IX.)

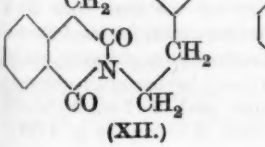
The *methyl* ester of the acid (IX) yields, on treatment with phosphorus oxychloride, a small quantity of a substance (m. p. 234°) which has the composition, $C_{17}H_{13}ON$, of oxyprotoberberine (X). The bright yellow colour of this substance is, however, not in accord with this structure and we are of the opinion that it is the *oxyisoprotoberberine* of the formula (XI; compare XVIII), but the detailed investigation of this substance was rendered difficult on account of the small yield obtained.

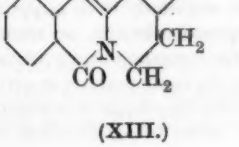
(X.)

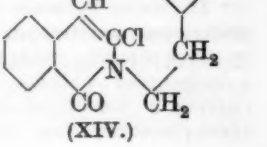



(XI.)

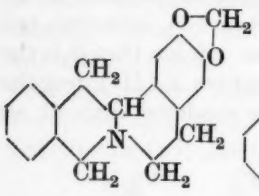
It is well known that derivatives of *iso*quinoline are formed with difficulty from unsubstituted β-phenylethylamine derivatives and that ring closure is much facilitated by the introduction of methoxy- or methylenedioxy-groups. With the view of obtaining increased yields of substances similar to those just described, a series of experiments was next carried out using homopiperonylamine (IA) in the place of β-phenylethylamine, and 2-*homopiperonylhomophthalimide* (XII) was readily obtained by condensing this with homophthalic acid. It is curious that this imide could not be converted into a substance of the oxyberberine type (XIII) by the action of dehydrating agents and also that, while the imide (IV) yields 1 : 3-dichloro*iso*quinoline (VI) on treatment with phosphorus oxychloride, the imide (XII) does not suffer disruption under these conditions but is converted into 3-*chloro*-2-*homopiperonyl*-1-iso*quinolone* (XIV). Attempts to convert this chloro-derivative into the substance (XIII) by treatment with copper powder and quinoline were unsuccessful.


(XII.)

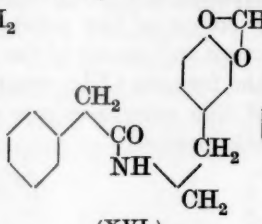

(XIII.)


(XIV.)

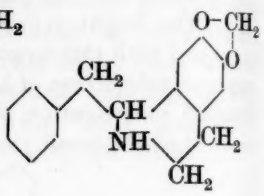
The imide (XII) is converted into the corresponding N-β-*homopiperonylhomophthalamic acid* (compare IX) on warming with alkali, and the investigation of the action of phosphorus oxychloride on the *methyl* ester of this acid has given interesting results. Two substances, *A* and *B*, are produced and of these, *A* (m. p. 180°), a colourless, feebly basic substance, has all the properties to be expected of 2 : 3-*methylenedioxyoxyprotoberberine* (XIII). It may be reduced electrolytically to the corresponding 2 : 3-*methylenedioxytetrahydroprotoberberine* (XV, m. p. 129°).



(XV.)



(XVI.)

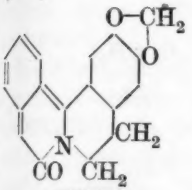


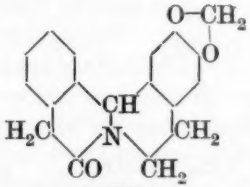
(XVII.)

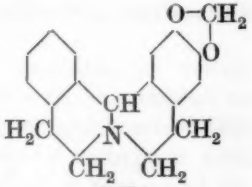
The correctness of the expression (XIII) for the substance *A* receives confirmation from the following independent synthetical experiments. *N*-Phenylacetylhomopiperonylamine (XVI), prepared by the method described by Decker (*Annalen*, 1913, **395**, 294), was converted, by treatment with phosphorus oxychloride, into 6 : 7-*methylenedioxy*-1-*benzyl*-3 : 4-*dihydroisoquinoline*, and this reduced to 1-*benzyl*nor*hydrohydrastinine* (XVII). This base, owing doubtless to the absence of methoxy-groups in the ring, does not condense with formaldehyde and hydrochloric acid, and heating with formaldehyde and formic acid in a sealed tube leads exclusively to the formation of the N-*methyl* derivative (benzylhydrohydrastinine, p. 1721). When, however, the *N*-formyl derivative of the base (XVII) is treated with phosphorus oxychloride, it yields 2 : 3-*methylenedioxydihydroprotoberberine* and this, on reduction, is converted into the tetrahydro-derivative, which melts at 129° and is identical with the substance (XV) produced by the reduction of *A*. Consequently, *A* must have the constitution (XIII).* The second substance, *B*, produced by the action of phosphorus oxychloride on the methyl ester of *N*-β-homopiperonylhomophthalamic acid (see above), has properties similar to those of oxy*iso*protoberberine (XI) and it is suggested that it is 2 : 3-*methylenedioxyoxy*iso*protoberberine* (XVIII). It is a

* If further evidence is required, it is supplied by the fact that 2 : 3-methylenedioxytetrahydroprotoberberine, on treatment with iodine followed by silver chloride, yields the corresponding protoberberinium chloride, which is decomposed by alkalis, in the same manner as ordinary berberinium chloride, yielding 2 : 3-methylenedioxydihydroprotoberberine and 2 : 3-methylenedioxyoxyprotoberberine, the latter being identical with *A* (compare p. 1723).

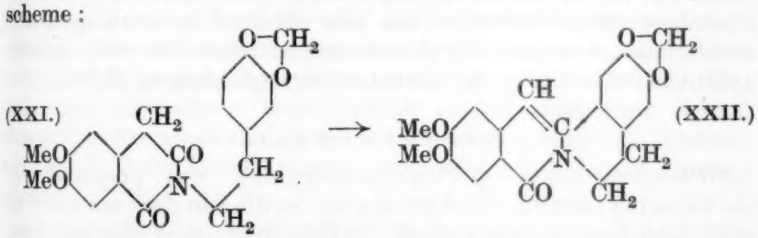
scarlet, crystalline substance (m. p. 225°), dissolving with difficulty in hydrolytic solvents, from which it separates in the hydrated form in orange needles which lose weight at 100° and are converted into the scarlet, anhydrous substance. On electrolytic reduction, the scarlet substance is first converted into the colourless 2 : 3-*methylenedioxyoxydihydroisoprotoberberine* (XIX) and then into 2 : 3-*methylenedioxytetrahydroisoprotoberberine* (XX) isomeric with the substance (XV).


(XVIII.)


(XIX.)


(XX.)

Synthesis of Oxy-ψ-berberine (compare Haworth, Perkin, and Rankin, J., 1924, **125**, 1691).—This synthesis, indicated by the scheme :

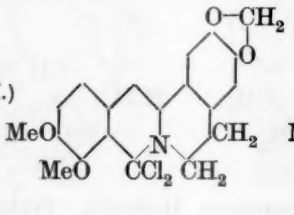

(XXI.) (XXII.)

was carried out in the following manner. 2-*Homopiperonyl*-6 : 7-*dimethoxyhomophthalimide* (XXI), prepared from 4 : 5-dimethoxyhomophthalic acid and homopiperonylamine, was converted, by hydrolysis with alkali, into the corresponding amic acid (compare IX). When the *methyl* ester of this acid was treated with phosphorus oxychloride, it gave a 70% yield of a substance melting at 268° which was identical with the oxy-ψ-berberine described by Haworth, Perkin, and Rankin. It is interesting that no isomeride of this substance could be detected in the product of the interaction of the methyl ester with phosphorus oxychloride. The imide (XXI), on treatment with phosphorus oxychloride, behaves similarly to 2-homopiperonylhomophthalimide (XII), yielding 3-*chloro*-2-*homopiperonyl*-6 : 7-*dimethoxy*-1-iso*quinolone* (compare XIV).

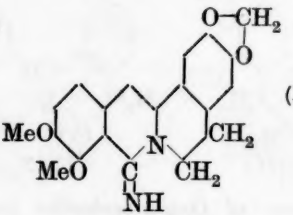
At the commencement of this research it became necessary to determine whether substances of the oxyberberine type are stable towards phosphorus oxychloride, that is to say, whether they are capable of formation in the presence of this reagent. Experiment showed that oxyberberine is readily acted on by phosphorus oxy-

chloride, two substances being formed, namely, methyl*nor*oxyberberine (Faltis, *Monatsh.*, 1910, **31**, 573; Bland, Perkin, and Robinson, J., 1912, **101**, 262; compare this vol., p. 744) and a chloro-derivative which clearly has the constitution (XXIII), because, when treated with ammonia, it yields *iminoberberine*, $C_{20}H_{18}O_4N_2$ (XXIV), a substance which does not melt at 280° and is characterised by the crystalline hydrochloride, $C_{20}H_{18}O_4N_2,HCl$, and by the fact that it is converted into oxyberberine on treatment with sodium hydroxide.

(XXIII.)



(XXIV.)



During the synthesis of oxy-ψ-berberine described above, a crystalline chloro-derivative was also obtained in small quantity which, since it yielded oxy-ψ-berberine on treatment with sodium hydroxide, was clearly the derivative corresponding to (XXIII).

Experimental.

β-*Phenylethylamine.*—β-Phenylpropionamide was prepared by the following method, which gives good results and does not seem to have been previously described. β-Phenylpropionyl chloride (prepared by boiling phenylpropionic acid with a slight excess of thionyl chloride and distilling the product under reduced pressure), dissolved in dry benzene, is saturated with dry ammonia, and the mixture of ammonium chloride and the amide recrystallised from hot water with the aid of animal charcoal. The amide separates in colourless leaflets (m. p. 105°) and is sufficiently pure for conversion into β-phenylethylamine by means of sodium hypochlorite (Decker, *Annalen*, 1913, **395**, 291).

β-3 : 4-*Dimethoxyphenylpropionic Acid.*—Veratraldehyde (100 g.), malonic acid (130 g.), and piperidine (5 c.c.) were heated in pyridine solution (250 c.c.) for 1½ hours on the steam-bath, during which rapid elimination of carbon dioxide took place, and the reaction was completed by boiling for 10 minutes. The product, on pouring into excess of dilute hydrochloric acid, gave an almost quantitative yield of 3 : 4-dimethoxycinnamic acid, which was reduced to 3 : 4-dimethoxyphenylpropionic acid by sodium amalgam under the conditions described by Perkin and Robinson (J., 1907, **91**, 1079).

2-β-*Phenylethylhomophthalimide* (IV).—β-Phenylethylamine hydrochloride (15·6 g.) is dissolved in water, the base liberated with potassium hydroxide, extracted with benzene, dried over potassium hydroxide, mixed with homophthalic acid (18 g.), and heated in an oil-bath at 180° for 3 hours. The product is dissolved in boiling alcohol and cooled, when the *imide* (IV) separates in almost colourless prisms (19 g.) and is sufficiently pure for most purposes. After a second crystallisation from alcohol, it was obtained in colourless prisms, m. p. 128—129° (Found: C, 77·0; H, 5·8. $C_{17}H_{15}O_2N$ requires C, 77·0; H, 5·7%).

2-β-Phenylethylhomophthalimide (IV) is insoluble in water, sparingly soluble in ether, and readily soluble in hot alcohol or acetic acid. It dissolves in sodium hydroxide to a yellow solution with a green fluorescence and is reprecipitated by saturation with carbon dioxide. If, however, the alkaline solution is warmed for several hours, the colour disappears and the imide is no longer precipitated by carbon dioxide.

The imide (1 g.) was heated in a sealed tube with phosphorus oxychloride (3 c.c.) at 140—150° for 3 hours, the excess of oxychloride removed by distillation under reduced pressure, the residue mixed with sodium hydroxide, and the solid collected. This substance crystallised from methyl alcohol containing animal charcoal in colourless needles (m. p. 123°) and was evidently identical with the 1 : 3-dichloro*iso*quinoline (VI) obtained by Gabriel (*loc. cit.*) (Found: C, 54·8; H, 2·6. Calc., C, 54·5; H, 2·5%).

2-β-*Phenylethyl*-4 : 4-*dimethylhomophthalimide* (V).—2-β-Phenylethylhomophthalimide (2 g.) was dissolved in a solution of sodium (0·35 g.) in alcohol (7 c.c.) and water (10·5 c.c.), methyl iodide (3 g.) added, and the mixture gently boiled until the green fluorescence had disappeared. Some of the alcohol was removed by distillation, the residue mixed with water, the precipitated oil extracted with ether, the extract dried over anhydrous magnesium sulphate, evaporated, and the oil distilled under 10 mm., when a colourless distillate was obtained which solidified on prolonged rubbing with petroleum (Found: C, 77·7; H, 6·5. $C_{19}H_{19}O_2N$ requires C, 77·8; H, 6·5%). This dimethyl derivative crystallises from aqueous alcohol in colourless needles (m. p. 60—61°) and is readily soluble in ether, but sparingly soluble in petroleum and insoluble in sodium hydroxide. That the methyl groups in (V) are both attached to carbon is shown by the fact that no methyl iodide is obtained when the substance is boiled with hydriodic acid.

2-β-*Phenylethyl*-3 : 4-*dihydro*-1-iso*quinolone* (VII). 2-β-Phenylethylhomophthalimide (2 g.), dissolved in a mixture of alcohol (60 c.c.) and concentrated sulphuric acid (40 c.c.), was placed in the

cathode compartment of an electrolytic cell, the cathode of which consisted of a piece of lead (150 sq. cm. surface) and the anode of a sheet of lead surrounded by sulphuric acid (20%). After a current of 5 amperes had been passed for 16 hours, the solution was diluted with water, extracted with chloroform, the extract dried over potassium carbonate, the solvent removed, and the residue crystallised from ether–petroleum (b. p. 40—60°), separating in colourless needles, m. p. 77—78° (Found: C, 81·3; H, 7·0. $C_{17}H_{17}ON$ requires C, 81·3; H, 6·8%). 2-β-*Phenylethyldihydroisoquinolone* is very soluble in organic solvents with the exception of petroleum, insoluble in dilute acids or alkalis, and will not condense with aldehydes in the presence of sodium ethoxide or piperidine.

2-β-*Phenylethyl*-1 : 2 : 3 : 4-*tetrahydroisoquinoline* (VIII).—The acid mother liquors from the preparation of the *iso*quinolone (see above) were made strongly alkaline with sodium hydroxide, extracted with chloroform, the extract dried over potassium carbonate, and the chloroform removed, when a basic oil remained which did not crystallise. This dissolved completely in dilute hydrochloric acid and, on concentrating, the *hydrochloride* crystallised; it separated from alcohol–ether in long, colourless needles, m. p. 227—229° (Found: C, 74·8; H, 7·4. $C_{17}H_{19}N,HCl$ requires C, 74·6; H, 7·3%).

N-β-*Phenylethylhomophthalamic Acid* (IX).—2-β-Phenylethylhomophthalimide (1·3 g.) was heated with *N*-sodium hydroxide (10 c.c.) for 12 hours on the steam-bath, when the imide dissolved and the yellow colour of the solution gradually disappeared. After cooling, the unchanged imide was precipitated by carbon dioxide, and the filtrate acidified with concentrated hydrochloric acid; the straw-coloured gum, which soon hardened, crystallised from benzene in colourless needles, m. p. 122—123° (Found: C, 72·2; H, 5·9. $C_{17}H_{17}O_3N$ requires C, 72·1; H, 6·0%). This acid is readily soluble in alcohol, ether, or benzene, sparingly soluble in water or petroleum, and dissolves in sodium bicarbonate with effervescence.

The *methyl* ester. When a methyl-alcoholic solution of the acid is saturated with dry hydrogen chloride, only a small yield of the methyl ester is obtained, the main product being the imide (IV), but the methyl ester may be obtained in a yield of 60% in the following way. The amic acid (2·8 g.), dissolved in a solution of sodium carbonate (0·53 g.) in water (50 c.c.), is mixed with a strong solution of silver nitrate (1·7 g.) and, after remaining for 2 hours in the dark, the silver salt is collected and thoroughly dried in a vacuum desiccator over sulphuric acid. The powdered salt, suspended in dry ether, is boiled under reflux with methyl iodide (2 g.) for 8 hours, and the solution is filtered and concentrated,

when the *methyl* ester separates in colourless prisms, m. p. 74—75° (Found: C, 72·9; H, 6·5. $C_{18}H_{19}O_3N$ requires C, 72·7; H, 6·4%).

Oxyisoprotoberberine (XI).—The above methyl ester (1 g.) was boiled with phosphorus oxychloride (2 c.c.) and toluene (5 c.c.) for an hour, hydrogen chloride being evolved and a brown gum separating. The product was diluted with petroleum (b. p. 40—60°; 100 c.c.), the clear liquid, which contained considerable quantities of the imide (IV), decanted, the brown gum dissolved in alcohol, mixed with sodium hydroxide, and the dark insoluble substance collected. It separated from glacial acetic acid in yellow needles, m. p. 234° (Found: C, 83·3; H, 5·2. $C_{17}H_{13}ON$ requires C, 82·6; H, 5·3%). *Oxyisoprotoberberine* is a weak base, dissolving in strong acids and being reprecipitated on dilution with water. It is sparingly soluble in organic solvents and its solutions in alcohol and glacial acetic acid exhibit an intense green fluorescence. The yield of this substance under the most favourable conditions is very small and in many experiments it could not be isolated at all.

2-*Homopiperonylhomophthalimide* (XII).—Homopiperonylamine was heated with homophthalic acid under conditions similar to those already described in the preparation of the imide (IV; p. 1715). The product separates from alcohol or glacial acetic acid in colourless needles, m. p. 156—157°, is insoluble in water, but dissolves in warm potassium hydroxide to a yellow solution with a green fluorescence which becomes gradually colourless on boiling (Found: C, 69·9; H, 4·8. $C_{18}H_{15}O_4N$ requires C, 69·9; H, 4·8%).

2-*Homopiperonyl*-4 : 4-*dimethylhomophthalimide* (compare V) was prepared as described on p. 1715 and on pouring into water, a crystalline precipitate separated which crystallised from methyl alcohol, in which it was sparingly soluble, in long, pale yellow, rectangular prisms, m. p. 126—127°. It is insoluble in aqueous alkali and could not be hydrolysed to the corresponding homophthalamic acid (Found: C, 71·3; H, 5·8. $C_{20}H_{19}O_4N$ requires C, 71·2; H, 5·6%).

3-*Chloro*-2-*homopiperonyl*-1-*isoquinolone* (XIV).—The imide (XII, 1 g.) was boiled with a mixture of phosphorus oxychloride (3 c.c.) and toluene (10 c.c.) for 6 hours, during which hydrogen chloride was evolved, and, on cooling, a brown syrup separated. After dilution with petroleum (b. p. 40—60°), the clear liquid (which contained unchanged imide and some chloro-derivative) was decanted and the residual oil dissolved in a little alcohol. Sodium hydroxide was then added to remove unchanged imide, and the insoluble solid collected and recrystallised from methyl alcohol, from which it separated in short needles, m. p. 128—129° (Found: C, 66·4; H, 4·3. $C_{18}H_{14}O_3NCl$ requires C, 66·1; H, 4·3%). When

this chloro-derivative was heated with copper powder in boiling quinoline solution and the quinoline removed by dilute hydrochloric acid, no trace of a condensation product could be isolated.

N-*Homopiperonylhomophthalamic Acid* (compare IX).—This acid was obtained from the imide (XII) by heating with *N*-sodium hydroxide (2 mols.) for 12 hours on the steam-bath. After saturation with carbon dioxide to remove unchanged imide, the filtered solution was acidified with concentrated hydrochloric acid, when a yellow gum separated which soon hardened, and crystallised from dilute acetic acid (1 : 1) in needles, m. p. 158—159° (Found: C, 66·1; H, 5·0. $C_{18}H_{17}O_5N$ requires C, 66·0; H, 5·2%). The *methyl* ester was prepared by the esterification of the acid with methyl alcohol and hydrogen chloride and also by the action of methyl iodide on the silver salt (compare p. 1716). It crystallises with difficulty and then separates from ether in long, colourless needles, m. p. 95—96° (Found: C, 67·1; H, 5·6. $C_{19}H_{19}O_5N$ requires C, 66·9; H, 5·5%).

The *amide* was prepared by dissolving the ester in ten times its weight of methyl alcohol and saturating with dry ammonia. The solution turned green and white needles of the imide (XII) separated; on diluting the filtrate with water, the amide was deposited as a crystalline mass, which separated from dilute methyl alcohol in needles, m. p. 216° (Found: N, 8·7. $C_{18}H_{18}O_4N_2$ requires N, 8·6%).

2 : 3-*Methylenedioxyoxyprotoberberine* (XIII).—The above methyl ester (3 g.), phosphorus oxychloride (6 c.c.), and toluene (15 c.c.) were boiled for an hour, cooled, diluted with petroleum (b. p. 40—60°), and the solvents (which contained the imide XII and some of the chloro-derivative XIV) decanted from the gum. The latter was extracted with boiling dilute hydrochloric acid, the insoluble portion dissolved in hot methyl alcohol and cooled, when a mass of almost colourless needles separated; a further quantity separated in fine needles on concentrating the acid extract, the filtrate from which contained the substance XVIII (see below). 2 : 3-*Methylenedioxyoxyprotoberberine* separates from methyl alcohol in colourless needles, m. p. 180°, and is sparingly soluble in ether, benzene, or cold alcohol, but readily soluble in hot alcohol or glacial acetic acid. It dissolves in concentrated mineral acids, but is reprecipitated on dilution with water (Found: C, 74·3; H, 4·6. $C_{18}H_{13}O_3N$ requires C, 74·2; H, 4·5%).

2 : 3-*Methylenedioxytetrahydroprotoberberine* (XV).—The substance XIII (1·5 g.), dissolved in alcohol (60 c.c.) and concentrated sulphuric acid (40 c.c.), was subjected to a current of 5 amperes for 20 hours in the cell described on p. 1716. The mixture was poured into water and extracted with chloroform, when some unchanged

XIII separated. The acid filtrate from this was made strongly alkaline with ammonia, extracted with chloroform, the extract dried over potassium carbonate, and the solvent removed, when a brown, syrupy base remained which yielded a sparingly soluble *hydrochloride*, crystallising from water in prisms, m. p. 270° (decomp.). The *base*, liberated from the hydrochloride by sodium hydroxide, separated from methyl alcohol in colourless needles, m. p. 128—129° (Found: C, 77·2; H, 6·1. $C_{18}H_{17}O_2N$ requires C, 77·4; H, 6·1%). The *picrate*, prepared in alcoholic solution, crystallises from alcohol in yellow needles, m. p. 208—210° (decomp.).

2 : 3-*Methylenedioxyoxyisoprotoberberine* (XVIII).—This highly coloured substance is contained in the acid mother-liquors obtained during the preparation of the substance XIII (see above). The liquors were evaporated and the residue was dissolved in glacial acetic acid containing a little acetic anhydride, when, after some time, a crystalline mass separated which was collected and boiled with water. The substance crystallises from dilute acetic acid in long, orange needles, which lose weight and become scarlet on drying on the steam-bath (compare p. 1713); m. p. 225—226° (Found: C, 74·5, 74·2; H, 4·8, 4·6. $C_{18}H_{13}O_3N$ requires C, 74·2; H, 4·5%). This substance is very sparingly soluble in alcohol, ether, or benzene, readily soluble in glacial acetic acid, and slightly soluble in water to a yellow solution. It is soluble in hot mineral acids, separating on cooling in orange needles which become scarlet on heating. The *acetate* separates from glacial acetic acid in pale yellow needles, m. p. 250° (decomp.), and is rapidly dissociated by water.

2 : 3-*Methylenedioxyoxydihydroisoprotoberberine* (XIX).—This substance was obtained when 2 : 3-methylenedioxyoxy*iso*protoberberine (XVIII) (1 g.), dissolved in a mixture of alcohol (60 c.c.) and concentrated sulphuric acid (40 c.c.), was reduced with a current of 5 amperes in the cell described on p. 1716. The original orange solution became almost colourless and, after pouring into water, this was extracted with chloroform (B), the extract dried over potassium carbonate, and the solvent removed, when a brown syrup remained which crystallised from alcohol in nodules, m. p. 196—197°, and from dilute acetic acid in needles, m. p. 203—204° (Found: C, 73·7; H, 5·2. $C_{18}H_{15}O_3N$ requires C, 73·7; H, 5·1%). This dihydro-derivative is sparingly soluble in the usual organic solvents, dissolves in concentrated mineral acids, and is reprecipitated by water.

2 : 3-*Methylenedioxytetrahydroisoprotoberberine* (XX).—The aqueous mother-liquors (B) from the chloroform extraction (see above) were made alkaline with ammonia and again extracted with chloroform, when a small amount of a basic substance was isolated. The yield of this substance was increased by continuing the above

reduction for 48 hours. The base is a syrup very soluble in organic solvents and has not been obtained in the crystalline state.

The *hydrochloride* is sparingly soluble and crystallises from dilute hydrochloric acid in small prisms decomposing at 260°. The *picrate*, prepared in methyl-alcoholic solution, crystallises from much methyl alcohol in long, yellow needles, m. p. 216—217° (Found: N, 11·2. $C_{24}H_{20}O_9N_4$ requires N, 11·0%).

2-*Homopiperonyl*-6 : 7-*dimethoxyhomophthalimide* (XXI).—This substance was prepared from homopiperonylamine and 4 : 5-dimethoxyhomophthalic acid as described on p. 1715 (Found: C, 65·0; H, 5·2. $C_{20}H_{19}O_6N$ requires C, 65·0; H, 5·1%). It is sparingly soluble in alcohol and crystallises from glacial acetic acid in pale yellow needles, m. p. 178—179°. It dissolves in warm sodium hydroxide to a yellow solution with a green fluorescence and is reprecipitated by carbon dioxide. The *dimethyl* derivative (compare V) was obtained by treating the imide with methyl iodide in alkaline solution under the conditions described on p. 1715. On pouring into water, a white solid separated which crystallised from methyl alcohol in colourless prisms, m. p. 151° (Found: C, 66·8; H, 5·9. $C_{22}H_{23}O_6N$ requires C, 66·5; H, 5·8%).

3-*Chloro*-2-*homopiperonyl*-6 : 7-*dimethoxy*-1-*isoquinolone* (compare XIV).—The above imide (1 g.) was heated with phosphorus oxychloride (2 c.c.) and toluene (5 c.c.) for 2 hours, during which hydrogen chloride was eliminated. Petroleum (b. p. 40—60°) was then added and, after standing for some time, the clear solution was decanted, the residue dissolved in alcohol, unchanged imide removed by treatment with sodium hydroxide, and the solid crystallised from glacial acetic acid, from which it separated in yellow needles, m. p. 163—164° (Found: C, 61·7; H, 4·7. $C_{20}H_{18}O_5NCl$ requires C, 61·9; H, 4·7%).

N-*Homopiperonyl*-4 : 5-*dimethoxyhomophthalamic Acid* (compare IX).—This was prepared by warming the imide with *N*-sodium hydroxide (2 mols.) for 12 hours on the steam-bath. On acidifying with concentrated hydrochloric acid, a grey, granular mass separated which crystallised from dilute acetic acid in needles, m. p. 181—182° (Found: C, 62·1; H, 5·5. $C_{20}H_{21}O_7N$ requires C, 62·0; H, 5·4%). The *methyl* ester, prepared by the two methods employed in the earlier cases (p. 1718), is sparingly soluble in ether and moderately soluble in methyl alcohol, from which it crystallises in colourless prisms, m. p. 136° (Found: C, 62·5; H, 5·6. $C_{21}H_{23}O_7N$ requires C, 62·8; H, 5·7%).

Oxy-ψ-berberine (XXII).—The above methyl ester (2 g.), phosphorus oxychloride (6 c.c.), and dry toluene (10 c.c.) were boiled for an hour, cooled, and diluted with petroleum (100 c.c.; b. p.

40—60°), and the clear solution decanted. The residue was washed with petroleum, digested with sodium hydroxide for 2 hours on the steam-bath, and the brittle solid boiled with a little alcoholic sodium hydroxide, collected, and crystallised from aqueous acetic acid, from which the substance separated in colourless needles, m. p. 267—268° (not depressed on admixture with a specimen of oxy-ψ-berberine prepared by Haworth, Perkin, and Rankin; *loc. cit.*). In several experiments a salt of the dichloro-derivative (compare XXIII) separated towards the end of the reaction as an orange-crystalline solid, which crystallised from methyl alcohol in orange-yellow needles, m. p. 204—205° (decomp.). It was soluble in water and, on treatment with sodium hydroxide and subsequent crystallisation from dilute acetic acid, gave oxy-ψ-berberine.

*Benzyl*nor*hydrohydrastinine* (XVII).—*N*-Phenylacetylhomopiperonylamine (XVI) (10 g.) was dissolved in toluene (50 c.c.) and boiled for 1½ hours with phosphorus oxychloride (20 c.c.). The solution was cooled, diluted with petroleum (b. p. 40—60°), the clear liquid decanted, the residual syrup dissolved in hot alcohol, acidified with sulphuric acid, and heated on the steam-bath with zinc dust until the intense blue fluorescence had disappeared. The solution was filtered hot, the zinc residues were thoroughly extracted with boiling water, and the base was liberated from the united filtrates by the addition of ammonia and extracted with benzene. The benzene extract was washed with water, dried over potassium hydroxide, and the benzene removed, when the residual syrup solidified to a pasty mass.

Benzyl*nor*hydrohydrastinine dissolves in the usual organic solvents with the exception of petroleum and crystallises from ether–petroleum in prisms, m. p. 64—66°. The *hydrochloride* separates from water in colourless, rectangular plates, m. p. 110°, and is sparingly soluble in water or alcohol and particularly sparingly soluble in dilute hydrochloric acid. The *picrate*, prepared in methyl-alcoholic solution, crystallises from methyl alcohol in short, thick prisms, m. p. 184—185° (Found: C, 55·3; H, 4·1. $C_{23}H_{20}O_9N_4$ requires C, 55·6; H, 4·0%). When the base was heated in methyl-alcoholic solution with formalin and diluted with water, an oil separated which was heated with hydrochloric acid, but no substance of the tetrahydroberberine type could be detected and the product contained large quantities of unchanged benzyl*nor*hydrohydrastinine hydrochloride.

Benzylhydrohydrastinine (p. 1712).—Benzyl*nor*hydrohydrastinine (XVII) (0·5 g.) was heated with water (5 c.c.), formic acid (1·2 c.c.), and formalin (1 g.) in a sealed tube for 8 hours at 180°. The product was diluted with water, made alkaline with sodium hydroxide, and

the solution decanted from the syrupy base. This was washed with water, and dissolved in hot dilute hydrochloric acid, when the *hydrochloride* of benzylhydrohydrastinine separated in colourless prisms, m. p. 174—175° (decomp.) (Found: C, 67·6; H, 6·2. $C_{18}H_{20}O_2NCl$ requires C, 68·0; H, 6·3%). The base, liberated from the hydrochloride, was a syrup which was not obtained in the crystalline state.

2 : 3 - *Methylenedioxydihydroprotoberberine.* — Benzyl*nor*hydrohydrastinine (5·4 g.) and anhydrous formic acid (1 g.) were heated in an oil-bath at 200° for 4 hours, the product dissolved in toluene (25 c.c.), and boiled with phosphorus oxychloride (10 c.c.) for 1½ hours. Light petroleum was added, the clear liquid decanted, the residue boiled with dilute hydrochloric acid and animal charcoal, filtered, and the filtrate concentrated, when clusters of yellow prisms of the hydrochloride separated. This was collected, dissolved in water, and the base liberated by sodium hydroxide as a pale yellow solid, which crystallised from ethyl alcohol in clusters of yellow needles, m. p. 128—129° (Found: C, 77·7; H, 5·5. $C_{18}H_{15}O_2N$ requires C, 77·9; H, 5·4%). The *hydrochloride* crystallises from dilute hydrochloric acid, in which it is sparingly soluble, in yellow prisms, m. p. 250°. The *picrate* separates from much alcohol or ethyl acetate in long, orange needles, m. p. 254—255°.

2 : 3-*Methylenedioxytetrahydroprotoberberine* (XV) was obtained by reducing the dihydro-derivative just described with zinc dust and sulphuric acid until the solution became colourless. The hot liquid was filtered, the filtrate decomposed by ammonia, the sticky base washed with water and crystallised from methyl alcohol, from which it separated in almost colourless needles, m. p. 128—129°. This base is identical with the substance resulting from the electrolytic reduction of 2 : 3-methylenedioxyoxyprotoberberine (XIII), since no depression in melting point was observed on mixing specimens which had been prepared by the two different methods.

The 2:3-*Methylenedioxyprotoberberinium Salts.*—The tetrahydrobase (XV), dissolved in alcohol, was oxidised by means of iodine in the presence of sodium acetate, when a yellow, crystalline precipitate separated, and, after concentrating, the precipitate was collected, suspended in water, and sulphur dioxide passed. The *iodide* obtained, crystallised from much water in long, pale yellow needles which did not melt at 300° (Found: C, 53·8; H, 3·5. $C_{18}H_{14}O_2NI$ requires C, 53·6; H, 3·5%). The corresponding *chloride* was obtained by digesting the iodide with silver chloride in aqueous suspension for some hours, filtering, and concentrating the filtrate, when the chloride separated as bright yellow needles which did not melt at 250°. When this chloride was heated for ½ hour with 50%

potassium hydroxide, a semi-solid mass separated which hardened on cooling. It was collected, ground, and extracted with hot, very dilute hydrochloric acid. The acid solution, make alkaline with ammonia, yielded a base which crystallised from alcohol in clusters of pale yellow needles, m. p. 128—129°, and proved to be identical with the 2 : 3-methylenedioxydihydroprotoberberine which had been previously obtained (p. 1722) by another process. The substance insoluble in the dilute hydrochloric acid was crystallised from dilute acetic acid, when colourless needles were obtained which melted at 180° and were identical with the 2 : 3-methylenedioxyoxyprotoberberine (XIII) described on p. 1718.

The Action of Phosphorus Oxychloride on Oxyberberine.—Oxyberberine (10 g.) was boiled with phosphorus oxychloride (50 c.c.) for 6 hours, during which the solution became deep orange and a bulky precipitate separated; the excess of oxychloride was then removed by distillation and the solid heated with dilute hydrochloric acid and filtered. The residue crystallised from glacial acetic acid in small, colourless needles, m. p. 245°, and was identical with a specimen of methyl*nor*oxyberberine which had been prepared from oxyberberine by heating with hydrochloric acid in a sealed tube (compare p. 1713). The orange-coloured acid filtrate was decomposed with a large excess of concentrated ammonia, and the *iminoberberine* (XXIV) crystallised from much alcohol, from which it separated in small, pale yellow needles which did not melt at 280° (Found : C, 68·1; H, 5·0. $C_{20}H_{18}O_4N_2$ requires C, 68·6; H, 5·2%). It is sparingly soluble in organic solvents and, on warming with sodium hydroxide, ammonia is evolved and oxyberberine separates. The *hydrochloride* was prepared by dissolving the base in warm dilute hydrochloric acid and allowing to cool slowly, when orange plates separated which did not melt at 280° (Found : C, 61·6; H, 4·9; N, 7·0. $C_{20}H_{19}O_4N_2Cl$ requires C, 62·2; H, 5·0; N, 7·2%). This hydrochloride dissociates slowly in contact with moisture and is rapidly changed to oxyberberine on treatment with sodium hydroxide.

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CCXXIX.—*Researches on Sulphuryl Chloride. Part III. The Influence of Catalysts on the Chlorination of Toluene.*

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The present investigation on the chlorination of toluene was undertaken with the object of increasing our knowledge of the influence of catalysts on the chlorinating properties of sulphuryl chloride, hitherto confined to the effect of the better known carriers on the chlorination of benzene (Silberrad, J., 1921, **119**, 2029; 1922, **121**, 1015).

Previous investigators have recorded that no action occurs between toluene and sulphuryl chloride below 115° (Dubois, *Bull. Acad. Roy. Belg.*, 1872, 42), but that at that temperature benzyl chloride and chlorotoluene are slowly formed. Tohl and Eberhardt (*Ber.*, 1893, **26**, 2940), working at 160°, also obtained a mixture of these compounds, whilst Wohl (D.R.-PP. 1467/1902, 160102/1902, and 162394/1903) patented the manufacture of benzyl chloride (and its homologues) by heating toluene (and its homologues) with sulphuryl chloride to temperatures not exceeding 130°, the yield claimed in the absence of light being 50% on the toluene used. Tohl and Eberhardt (*loc. cit.*) also observed that iodine (at 160°) exercised no retarding influence on the formation of benzyl chloride; and Witte (*Pharm. Rec.* of New York, 1889, Dec. 16), Tohl and Eberhardt (*Ber.*, 1893, **26**, 2943), and Böeseken (*Rec. trav. chim.*, 1911, **30**, 381) obtained *o*- and *p*-toluenesulphonyl chloride as the chief product of treating toluene with sulphuryl chloride in the presence of aluminium chloride.

Apart from the simultaneous formation of chlorotoluene and benzyl chloride the present investigation has not confirmed these observations. The two ingredients react to a noticeable extent far below 115° in the absence of either light or catalysts, whilst iodine exercises a marked effect at 70° both by inhibiting side-chain substitution and by accelerating the formation of chlorotoluene. As regards the influence of aluminium chloride, toluenesulphonyl chloride or chlorotoluene can be produced at will according as the conditions selected are conducive to the Friedel and Crafts reaction or to chlorination; the former conditions appear to have been those selected by the above cited previous workers and the latter come within the present investigation (compare No. 3).

The catalysts examined may conveniently be divided into groups: those which either inhibit chlorination or alter its course without inducing any appreciable acceleration, and those which accelerate

substitution. Of the first series, phosphorus pentachloride is the most remarkable; it appears to prevent ring substitution altogether without, however, materially influencing the quantity of benzyl chloride produced in a given time.* Manganese chloride and arsenic also exhibit this peculiarity, though to a lesser extent, whilst the latter also accelerates side-chain substitution. All the other catalysts examined accelerate ring substitution and, with the exception of sulphur † and bromine, at the expense of the benzyl chloride produced, the yield of the latter compound being reduced to zero in the case of iron, aluminium, antimony, bismuth and tellurium.

Further, the catalytic activity of the elements of the same group, with the exception of bromine, is a function of the atomic weight, increasing with this apparently up to a maximum, as illustrated by bismuth (see table on p. 1726). In this respect, therefore, the elements examined behave in the same manner as halogen carriers in direct chlorination (Willgerodt, *J. pr. Chem.*, 1886, **33**, 264), from which it would appear that they operate as chlorine carriers rather than as dissociation catalysts. The only exception to Willgerodt's rule is furnished by bromine, which is much more active than iodine in spite of their relative atomic weights. It is suggested that this abnormality is due to the transient formation of sulphuryl bromide, concerning the existence of which there has been so much controversy (Odling, *Quart. J. Chem. Soc.*, 1854, **7**, 2; *Jahresbericht*, 1854, 308; *Handbuch Deutsch von Oppenheim*, 1865, **1**, 169; also Sestini, *Bull. Soc. chim.*, 1868, **10**, 226; Gustavson, *Ber.*, 1873, **6**, 9; Melsens, *Compt. rend.*, 1873, **76**, 92). This suggestion is borne out by the fact that bromine shows this abnormal activity only if previously dissolved in and added with the sulphuryl chloride and not when admixed with the hydrocarbon (Nos. 14 and 15), whereas with iodine, which admittedly shows no tendency to form sulphuryl iodide (compare Sestini, *loc. cit.*; Odling, *loc. cit.*), it makes but little difference whether it be added to the hydrocarbon or to the sulphuryl chloride (Nos. 16 and 17).

Not only is the intensity of the action a function of the atomic weight, but also the nature of the chlorination effected (see table); thus, the elements of the same group show a decreasing tendency to induce side-chain substitution with increasing atomic weight, but an increasing tendency to accelerate ring substitution. In all cases where the catalyst showed a marked influence the reaction was accompanied by the formation of strongly coloured inter-

* Erdmann (*Annalen*, 1893, **272**, 149), working with chlorine, found that phosphorus pentachloride accelerated side-chain substitution.

† This observation is in accord with Beck's work on the direct chlorination of toluene in the presence of sulphur (*Ber.*, 1892, **25**, 2445).

mediate products the constitution of which is evidently similar to those previously observed in the case of benzene, thus again contributing strong evidence in favour of the additive theory of chlorination (Silberrad, *loc. cit.*).

Comparative Action of Catalysts of the Same Periodic Group.

		Products obtained on boiling for 8 hours.				
Element.	At. wt.	% of chlorine in product.	% of chloro-toluene produced.	% of benzyl chloride produced.	Ratio chloro-toluene to benzyl chloride.	Coloration.
Group V.						
Phosphorus	31·04	2·1	nil	7·6	0·0	Nil
Arsenic ...	74·96	4·6	3·3	12·6	0·25	Amber
Antimony	120·2	26·2	93·1	nil	∞	Dark brown
Bismuth ...	208·0	21·1	76·4	nil	∞	Dark brown
Group VI.						
Sulphur ...	32·07	18·1	50·5	13·8	3·7	Pale amber
Selenium	79·2	23·2	77·0	5·2	14·8	Dark amber
Tellurium	127·5	25·1	89·1	nil	∞	Deep brown
Group VII.						
Bromine ...	79·92	10·8	26·9	11·3	1·3	—
Iodine	126·92	5·6	16·0	4·5	3·5	—

EXPERIMENTAL.

For the sake of brevity the method of procedure adopted is described in general terms and the quantitative results are summarised at the end of the paper, only peculiarities specific to each catalyst being described under that head. Unless stated otherwise, no coloration developed.

The apparatus and the method used were similar to those described by one of us (Silberrad, J., 1921, **119**, 2031), save that the mixture was boiled for 8 hours and light was found to produce so marked an effect on the results that its influence was rigidly excluded. The hydrocarbon (79 c.c. of toluene) was treated with 10% excess of sulphuryl chloride (66 c.c.) in the presence of the desired catalyst. The product was boiled with 250 c.c. of water * and steam-distilled, and the distillate dried and fractionated. The fraction boiling below 180° was freed from traces of dichloro-compounds by redistillation and its composition then calculated from its density and the quantity of benzyl chloride present, estimated by boiling a weighed quantity with excess of solid silver nitrate and sufficient alcohol to form a boiling saturated solution (compare Schultze, *Ber.*, 1884, **17**, 1675; Cohen, Dawson, Blockey, and Woodmansey, J., 1910,

* Without this preliminary treatment sulphuryl chloride when present in any quantity passed over undecomposed on steam distillation.

97, 1625); a less concentrated solution of silver nitrate is liable to give inaccurate and erratic results.

No. 1. *Catalyst nil.*—The boiling ingredients slowly evolved sulphur dioxide and hydrogen chloride: the reaction was evidently not completed during the experiment (8 hours).

No. 2. *Catalyst Gold Chloride.*—Gold is apparently not attacked by sulphuryl chloride below about 150° (North, *Bull. Soc. chim.*, 1911, **9**, 646). It was therefore introduced as the anhydrous trichloride (1·3 g.). The velocity of chlorination was thereby raised about 30% without, however, appreciably altering the nature or relative proportion of the products. The reacting mixture assumed an amber tint.

No. 3. *Catalyst Aluminium Chloride* (*anhydrous*).—Aluminium chloride combines with sulphuryl chloride in the absence of moisture to form aluminium chlorosulphoxide, which acts as a powerful dissociation catalyst (Adrianowsky, *Ber.*, 1879, **12**, 688; Ruff, *Ber.*, 1902, **35**, 4453; *Chem. Ztg.*, 1906, **30**, 1225; Rohland, *Chem. Ztg.*, 1906, **30**, 1173; Silberrad, J., 1921, **119**, 2031). The anhydrous compound was therefore used, 14 g. being added to the toluene and the required quantity of sulphuryl chloride run into the mixture previously raised to 70°. A vigorous evolution of sulphur dioxide and hydrogen chloride took place at once and the reaction was completed in 2½ hours. The acceleration effected by this catalyst therefore amounted to approximately 1600%. The product, which was at first deep purple and finally dark vandyke-brown, had the characteristic odour of toluenesulphonyl chloride. The quantity was, however, small, chlorination being almost the only reaction under the above conditions.

No. 4. *Catalyst Carbon.*—Carbon is not attacked by sulphuryl chloride (Heinemann and Köchlin, *Ber.*, 1882, **15**, 1736; *Jahresbericht*, 1882, 234); any influence this substance might exercise was therefore likely to be physical rather than chemical. Finely-ground (200-mesh) wood charcoal was used (0·7 g.). A slight increase in the amount of nuclear substitution appeared to be induced.

No. 5. *Catalyst Stannic Chloride.*—Tin is only slowly attacked by sulphuryl chloride (Heinemann and Köchlin, *loc. cit.*), anhydrous stannic chloride (14 g.) was therefore used. Substitution took place almost entirely in the ring. The reacting products developed a faint pink tint.

No. 6. *Catalyst Phosphorus Pentachloride.*—In order to avoid complication arising from the possible formation of sulphur chloride *

* Sulphuryl chloride converts phosphorus into the trichloride (Köchlin and Heinemann, *Ber.*, 1881, **15**, 1736) and less readily into the pentachloride (North and Thompson, *J. Amer. Chem. Soc.*, 1918, **40**, 774), whilst the latter

the pentachloride (0·7 g.) was used. Chlorination proceeded even more slowly than without the catalyst, and the action was restricted entirely to side-chain substitution.

No. 7. *Catalyst Arsenic.*—Arsenic is rapidly converted into the trichloride by sulphuryl chloride (Köchlin and Heinemann, also Ruff, *loc. cit.*), The finely-ground element (0·7 g.) was therefore used. The reaction proceeded slowly, substitution occurring chiefly in the side chain.

No. 8. *Catalyst Antimony.*—Antimony reacts with sulphuryl chloride, forming the trichloride (Köchlin and Heinemann, *loc. cit.*). The element (0·7 g.) was therefore used. A steady and vigorous evolution of gas took place during the whole of the experiment, and the reaction was practically completed in 3 hours. The acceleration caused by this catalyst therefore amounted to 1300% approximately. The product, initially purple, gradually turned deep vandyke-brown. Substitution took place entirely in the ring.

No. 9. *Catalyst Bismuth.*—The action of sulphuryl chloride on this metal does not appear to have been previously examined. It dissolves readily, however, and was therefore introduced in the metallic form (0·7 g.). A vigorous action set in and a steady evolution of gas continued during the whole of the experiment. As a catalyst, bismuth behaves very similarly to antimony; the reaction mixture also passes through a precisely similar series of colour changes and substitution occurs wholly in the ring.

No. 10. *Catalyst Sulphur Chloride.*—According to Heinemann and Köchlin (*loc. cit.*) sulphuryl chloride does not act on sulphur at all; Ruff (*loc. cit.*), however, observed the formation of sulphur monochloride at 200°, and North and Thompson (*J. Amer. Chem. Soc.*, 1918, **40**, 774) observed it at 95—98°. Preliminary experiments with toluene showed that the hydrocarbon was very little attacked during the first 5 or 6 hours when elementary sulphur was used, but that after that the reaction proceeded just as rapidly as when sulphur chloride was added, thus proving beyond a doubt that sulphur is slowly converted into sulphur monochloride even at 70°. In order to avoid complication, therefore, the catalyst was intro-

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substance reacts with a further quantity of sulphuryl chloride with formation of thionyl chloride, phosphorus oxychloride, and chlorine (Michaelis, *Jenaische Z. Med. Naturwiss.*, 1871, **6**, 79; *Z. Chemie Pharm.*, von Beilstein Fittig u. Hubner, 1871, **6**, 460). The thionyl chloride reacts with a further quantity of phosphorus trichloride, producing phosphorus sulphur chloride (Michaelis, *Z. Chem. Pharm.*, von Beilstein Fittig u. Hubner, 1871, **6**, 151), which in its turn is reconverted into phosphorus pentachloride and sulphur chloride by a further quantity of sulphuryl chloride (Michaelis, *loc. cit.*; compare also North and Thompson, *loc. cit.*); hence the risk of complications through the formation of sulphur chloride.

duced in the form of sulphur chloride (0·7 g.). A steady and fairly strong reaction took place during the whole experiment, the amount of side-chain substitution being doubled and that in the ring quadrupled by this catalyst. The reacting liquid assumed a pale amber tint.

No. 11. *Catalyst Selenium.*—Selenium is rapidly attacked by sulphuryl chloride with formation of the tetrachloride (Lehner and North, *J. Amer. Chem. Soc.*, 1907, **29**, 33). The element (0·7 g.) was therefore used. A vigorous reaction proceeded throughout the experiment and the product assumed a dark amber colour.

No. 12. *Catalyst Tellurium.*—Tellurium is converted first into the di-, then into the tetra-chloride on heating with sulphuryl chloride (Lenher, *J. Amer. Chem. Soc.*, 1898, **30**, 737). The element (0·7 g.) was therefore used. The reaction was perceptibly more vigorous than with selenium, chlorination being complete in 5 hours and substitution taking place almost entirely in the nucleus. The mixture, too, assumed a much darker tint, changing from a dull purple-brown in the early stages to a very dark amber-brown at the end.

No. 13. *Catalyst Manganese Chloride.*—The manganese was introduced as anhydrous iron-free manganous chloride, in the presence of which chlorination appeared to proceed even more slowly than without any addition.

No. 14. *Catalyst Bromine* (added to the hydrocarbon).—Sulphuryl chloride decomposes hydrogen bromide with liberation of bromine, but then the reaction appears to stop (Besson, *Compt. rend.*, 1896, **122**, 467). In conformity with this observation it was found that bromine added to the hydrocarbon exercised little or no influence on the rate of chlorination.

No. 15. *Catalyst Bromine* (added to the sulphuryl chloride).—Having regard to the possibility of the intermediate formation of sulphuryl bromide, Experiment No. 14 was repeated, bromine being added to the sulphuryl chloride instead of the hydrocarbon. The reaction was much more vigorous, approximately double the amount of substitution occurring in 8 hours.

No. 16. *Catalyst Iodine* (added to the hydrocarbon).—According to Ruff (*Ber.*, 1901, **34**, 1749) sulphuryl chloride alone is without action on iodine. On prolonged boiling, however, a dilute solution of iodine in sulphuryl chloride became colourless, presumably due to the formation of iodine chloride. Added to the hydrocarbon, iodine (0·7 g.) accelerated ring substitution to a small extent at the expense of the benzyl chloride formed.

No. 17. *Catalyst Iodine* (added to sulphuryl chloride).—Unlike bromine, iodine (0·7 g.) added to the sulphuryl chloride produced a

similar result to that obtained when the halogen was added to the hydrocarbon.

No. 18. *Catalyst Iron.*—According to North (*Bull. Soc. chim.*, 1911, **9**, 646), who obtained ferric chloride by heating iron with sulphuryl chloride to 160°, this metal is attacked by sulphuryl chloride with some difficulty. Heated in the presence of the hydrocarbon, however, it (0·7 g.) rapidly passed into solution and induced vigorous substitution in the nucleus. The reacting mixture assumed a dark olive-green colour.

No. 19. *Catalyst Platinum.*—According to North (*loc. cit.*) platinum behaves like iron when heated with sulphuryl chloride. The finely divided metal (0·7 g. of 20% platinum asbestos) was therefore used. The bulk of the platinum gradually passed into solution and exercised a slight accelerating influence.

TABLE.

Giving Quantitative Results obtained by boiling 0·75 *g.-mol. of Toluene with* 10% *excess Sulphuryl Chloride for* 8 *hours in the presence of Various Catalysts.*

		Products obtained.							
			Steam-distilled product.		Fractionated product.				
							Composition.		
No.	Catalyst.	Crude product. Yield c.c.	Yield c.c.	$d_{4°}^{16°}$.	Yield c.c.	$d_{4°}^{16°}$.	Toluene %.	Chloro-toluene %.	Benzyl chloride %.
1	Nil	80	73	0·921	60	0·905	80·3	12·8	6·9
2	Gold chloride	76	70	0·927	59	0·918	73·5	17·0	9·5
3	Aluminium chloride*	79	69	1·084	58·5	1·073	3·1	96·9	nil
4	Carbon	79	76	0·914	67·5	0·912	76·5	16·9	6·6
5	Stannic chloride ...	80	78	0·924	66·5	0·914	74·5	24·8	0·7
6	Phosphorus penta-chloride	80	77	0·900	62·5	0·880	92·4	nil	7·6
7	Arsenic	78	75	0·907	64·5	0·898	84·1	3·3	12·6
8	Antimony*	78	75	1·067	65·5	1·063	6·9	93·1	nil
9	Bismuth	80	78	1·027	63·2	1·022	23·6	76·4	nil
10	Sulphur chloride ...	79	76	1·010	62	0·997	35·7	50·5	13·8
11	Selenium	82	80	1·046	71	1·037	17·8	77·0	5·2
12	Tellurium*	80	79	1·069	71	1·053	10·9	89·1	trace
13	Manganese chloride	78	75	0·892	64·5	0·885	91·2	2·2	6·6
14	Bromine (added to hydrocarbon) ...	80	77	0·917	65	0·905	80·4	11·0	8·6
15	Bromine (added to SO_2Cl_2)	79	74	0·948	65·5	0·941	61·8	26·9	11·3
16	Iodine (added to hydrocarbon) ...	80	76	0·913	68·5	0·901	81·9	16·5	1·6
17	Iodine (added to SO_2Cl_2)	80	77	0·918	69·5	0·906	79·5	16·0	4·5
18	Iron	81	77	1·022	68	1·017	25·7	74·3	nil
19	Platinum	75	72	0·944	59	0·940	61·8	34·9	4·3

* In the presence of these catalysts the reaction was completed in less than 8 hours, namely, with aluminium chloride in 2½ hours, with antimony in 3 hours, and with tellurium in 5 hours.

Our thanks are due to Messrs. A. Boake Roberts & Co., Ltd., of Stratford, for supplying the sulphuryl chloride required for this investigation.

THE SILBERRAD RESEARCH LABORATORIES,
BUCKHURST HILL, ESSEX. [*Received, May 1st*, 1925.]

CCXXX.—*Stereoisomeric Azo-dyes.*

By GILBERT T. MORGAN and DONAL GEORGE SKINNER.

A STUDY of the absorption of asymmetric substances by animal fibres was made by Willstätter (*Ber.*, 1904, **37**, 2758), who employed racemoid alkaloids but without finding any preferential absorption of one optical component by wool or silk.

Porter and Hirst (*J. Amer. Chem. Soc.*, 1919, **41**, 1264) prepared a varied series of asymmetric azo-dyes with the object of establishing a definite relationship between the chemical structures of dyes and their function as vital stains. They report, but without giving practical details, one case of a racemoid dye on which wool acted selectively, absorbing more of the lævo- than of the dextro-isomeride. Their azo-dyes, which contained an asymmetric carbon atom derived from *p*-aminobenzhydrol and the *p*-aminodiphenylalkylcarbinols, $NH_2 \cdot C_6H_4 \cdot CAlk(OH) \cdot C_6H_5$, were prepared by successively diazotising these amines and coupling the diazonium salt with β-naphthol, dimethylaniline, naphtholsulphonic acids, or naphthylaminesulphonic acids.

Ingersoll and Adams (*J. Amer. Chem. Soc.*, 1922, **44**, 2930) obtained *d*- and *l*-forms of *p*-aminobenzoyl-α-aminophenylacetic acid and converted these into two pairs of optically active dyes by diazotising and coupling with β-naphthol and dimethylaniline. The β-naphthol dyes were absorbed by wool in equal amounts, whereas the two dimethylaniline dyes were absorbed at unequal rates.

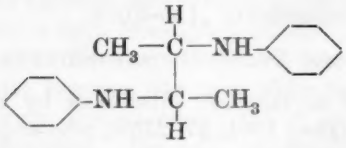
Racemoid aminomandelic acid was resolved by Porter and Ihrig through its cinchonine salt and its optically active components were diazotised and coupled with β-naphthol. When wool was dyed with a racemoid mixture of these azo-colouring matters, the dye-bath became lævorotatory owing to the higher rate of absorption of the dextro-form (*J. Amer. Chem. Soc.*, 1923, **45**, 1090).

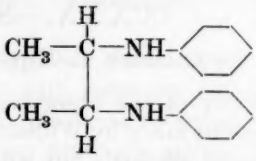
In the experiments described below, two sets of stereoisomeric dyes were prepared and their enantiomorphous components were isolated.

n-Butyl alcohol, kindly supplied by Captain Desborough of the

Royal Naval Cordite Factory, was converted successively into β-butylene and βγ-dibromo-*n*-butane. The last product was then condensed with aniline, whereby two stereoisomeric bases were obtained, but the *dl*-diamine (I) was in much larger yield than its *meso*-isomeride (II). The preparation was substantially that carried out by Trapesonzjanz (*Ber.*, 1892, **25**, 3280), although this investigator did not recognise the two stereoisomerides.

(I.)

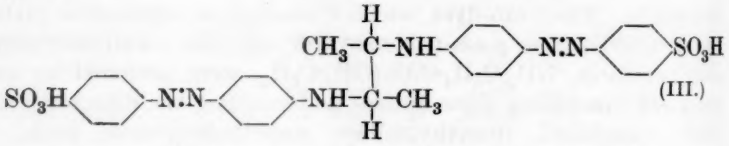




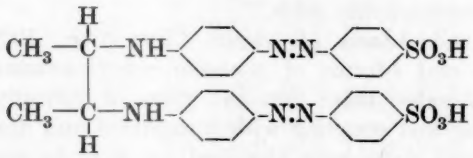
(II.)

Both stereoisomeric bases were oily, but of their solid derivatives it was found that those of the *meso*-diamine were less fusible and less soluble than those of the *dl*-isomeride.

The two diamines were separated by means of their crystallisable salts (nitrate, sulphate, picrate) and were coupled separately with diazotised sulphanilic acid, when two stereoisomeric azo-dyes were obtained.



(III.)



(IV.)

These disazo-dyes retain the "tartaric acid" configuration of the original bases. The compound IV from the *meso*-diamine was non-resolvable, whereas its isomeride III was resolved into optically active forms by means of the strychnine and cinchonidine salts.

The conditions under which solutions of the racemoid dye were kept in contact with wool for a prolonged interval at 20° were varied as to solvent, time of contact, and strength of solution, but only in one case was a slight optical activity observed in the dye-bath. The rates of absorption by wool of the four stereoisomeric dyes—the *dl*-, *d*-, *l*-, and *meso*-forms—were then investigated, and in all four cases the solutions of the dyes were of the same strength, the volume of the solution being proportional to

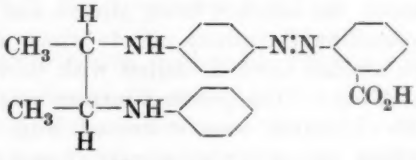
the weight of wool employed. At fixed intervals of time the amount of colouring matter remaining in solution was titrated by standard titanous chloride, this estimation giving a measure of the dye absorbed. The dextrorotatory dye was absorbed by the fibre at a slightly faster rate than the racemoid compound, whereas the lævorotatory isomeride was absorbed more slowly than either.

Although the differences in the measured rates of absorption of these three stereoisomeric forms were small, they were consistent for all the readings taken. The faster absorption of the *d*-compound was in agreement with the qualitative observation that a solution of the racemoid dye on prolonged contact with wool tended to become lævorotatory. The smallness of this optical activity had indicated that the differences in the rates of dyeing of the two enantiomorphs would also be small; the qualitative experiments confirm this anticipation and the greater rate of absorption of the *dextro*-form is also in agreement with the results of Porter and Ihrig (*loc. cit.*).

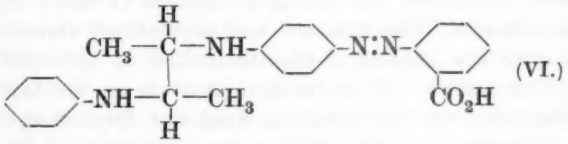
The *meso*-isomeride was found to dye wool at a much slower rate than any of its three stereoisomerides, this being the first case in which internally and externally compensated disazo-dyes have been contrasted.

Attempts were next made to demonstrate selective absorption by wool of less acidic colouring matters containing carboxyl groups and accordingly *dl*- and *meso*-diphenyl-βγ-diamino-*n*-butanes were coupled with diazotised anthranilic acid, when it was found that these diamines coupled with only one molecular proportion of the diazo-compound so that the resulting monoazo-dyes no longer retained any analogy with tartaric acid.

The *cis*- and *trans*-carboxyazo-dyes from the *meso*- and *dl*-diamines are represented respectively by formulæ V and VI, both being resolvable.



(V.)



(VI.)

Attempts were made with several alkaloids to resolve the latter more plentiful dye, dl-trans-2-*carboxybenzene*-4-*azodiphenyl*-βγ-*di*-

amino-n-*butane*, into its enantiomorphs, but only the lævorotatory isomeride was obtained and that through the agency of the strychnine salt.

The rates of absorption by wool of the three stereoisomerides, when ascertained by the titanous chloride titration, showed that, as in the case of the sulphonated disazo-dyes, the *lævo-trans*-compound was absorbed less readily than the *dl-trans*-isomeride, the differences being greater than those observed with the sulphonated dyes. The rates of absorption for the two racemoid, *cis*- and *trans*-carboxylated azo-dyes were practically identical.

Experimental.

*Stereoisomeric Diphenyl-*βγ*-diamino*-n-*butanes.*

The vapour of *n*-butyl alcohol was passed through a mixture of sand and phosphoric acid at 300—350° contained in a cylindrical copper vessel, and to the distillate of crude β-butylene, condensed and cooled with ice and salt, was added bromine drop by drop so that only a slight excess of halogen was present. The dibromide, washed with aqueous alkali and dried, was distilled fractionally until βγ-dibromo-*n*-butane was isolated, b. p. 157—158° (J., 1923, **123**, 97).

Aniline (600 g.) and 60 g. of βγ-dibromide were heated together at 160° for 4 hours, when the mixture became pasty owing to the separation of hydrobromides. After neutralisation with saturated aqueous sodium carbonate the mixture was distilled in steam to remove excess of aniline, and the residue extracted with benzene or ether. The crude diamines left on evaporating the solvent weighed 50 g. (yield 74%, calculated on βγ-dibromide).

dl-*Diphenyl-*βγ*-diamino*-n-*butane* (I).—The crude bases, consisting mainly of *dl*-diamine and a small proportion of *meso*-diamine, were dissolved in 50 c.c. of alcohol, 50 c.c. of nitric acid (*d* 1·42), and 100 c.c. of water, the solution being stirred and cooled in ice and salt. The crystalline *dl*-diamine nitrate which separated was recrystallised from alcohol until it melted with decomposition at 170—175° (weight 37 g.). The purified nitrate was decomposed with ammonia, the liberated base extracted with benzene and precipitated as picrate by adding picric acid (1 mol.) dissolved in the same solvent. The product was crystallised repeatedly from benzene until the purified *dl*-picrate melted at 136—137° (weight 36 g.). This method of purification depends on the fact that the small proportion of *meso*-diamine does not form a crystallisable picrate. Alternatively the *dl*-base may be purified by repeated crystallisation of its sulphate. This diamine, liberated by ammonia from its nitrate, was extracted with benzene, dissolved in alcohol,

and treated with the calculated amount of 30% sulphuric acid. The sulphate which separated was crystallised repeatedly from alcohol until a constant melting point—182°—was attained (Found: S, 9·4. $C_{16}H_{20}N_2,H_2SO_4$ requires S, 9·5%).

meso-*Diphenyl*-βγ-*diamino*-n-*butane* (II).—The *meso*-diamine, formed only in small amount by the condensation of βγ-dibromo-*n*-butane and aniline, is present together with *dl*-isomeride in the mother-liquors from the nitrate and picrate of the latter base. It was set free in the solutions by ammonia and extracted with benzene. The crude diamines obtained after concentrating the benzene extract weighed 21 g. and were converted into sulphate with 30% sulphuric acid, when the crystalline product obtained was *dl*-diamine sulphate. The filtrate was cooled and treated with dilute aqueous sodium nitrite; the viscid, brownish-yellow nitrosoamine was removed with ether and crystallised from petroleum (b. p. 80—100°) until it separated in pale yellow, arborescent growths of the purified *meso*-butylene-βγ-diphenyldinitrosoamine, m. p. 125°. A small amount of uncrystallisable oily residue was left consisting of the mixed *dl*- and *meso*-dinitrosoamines.

The dinitrosoamine was reduced with tin and hydrochloric acid in hot alcoholic solution, and the solution containing the stannichloride of the diamine was rendered alkaline with sodium hydroxide until the tin hydroxides redissolved. The oily diamine was extracted with benzene (yield 37%) and converted into its sulphate, which crystallised from alcohol and melted at 206°. This sulphate was not only less fusible but also less soluble in alcohol than the sulphate of the *dl*-diamine. The latter property was utilised in an alternative separation. Sulphate mother-liquors rich in *meso*-diamine were rendered alkaline with ammonia, extracted with benzene, the base converted into sulphate, and this salt crystallised repeatedly from alcohol until it melted at 206° (Found: S, 9·5. $C_{16}H_{20}N_2,H_2SO_4$ requires S, 9·5%).

Azo-dyes from Diphenyl-βγ-*diamino*-n-*butane.*

dl-*Di*-4′-*sulphobenzenedis*-4-*azodiphenyl*-βγ-*diamino*-n-*butane* (III).—*dl*-Diphenyl-βγ-diamino-*n*-butane (3·5 g.; 1 mol.), dissolved in 3·5 c.c. of concentrated hydrochloric acid and 10 c.c. of water, was added gradually to a solution of benzene-*p*-diazoniumsulphonate prepared from 5 g. of sulphanilic acid (2 mols.); a dark red disazo-dye separated (8 g. or 91%). This product dissolved readily in alcohol or glacial acetic acid, but was less soluble in acetone and insoluble in other organic solvents or water; it was dissolved in the minimum amount of dilute ammonia and reprecipitated by acid as a dark red, amorphous powder with bronzy reflex. The

dye developed intensely red colorations with concentrated mineral acids, had no definite melting point, but decomposed at 194°.

The *potassium* salt, obtained as a viscid solid by concentrating the solution of the dye in aqueous potassium carbonate, crystallised in an anhydrous form from dilute alcohol in small, orange needles (Found: K, 11·5; S, 9·3; azo-N_2 by titanous chloride, 8·1. $C_{28}H_{26}O_6N_6S_2K_2$ requires K, 11·4; S, 9·35; azo-N_2, 8·2%).

Dyeing Properties of the Racemoid Colouring Matter.—In the presence of sodium sulphate and sulphuric acid the dye liberated from its potassium salt in dilute solution dyed wool in deep orange shades, the colour being stripped by ammonia or strong soap solution.

Silk was dyed in boiled-off liquor and developed in a 1% sulphuric acid bath, giving golden-yellow shades. The partially exhausted solutions were examined in the polarimeter, a 12-volt, 24-watt Siemens lamp being used as a source of light (the wave-length being 6708 Å.). No activity was developed in the dye-bath whether the solvent employed was water, dilute alcohol, or 30% acetic acid, the strength of the dye-bath being approximately 0·75%.

In their successful attempt to show selective action of wool on a racemoid dye Porter and Ihrig (*loc. cit.*) used glacial acetic acid as solvent. The dye was employed in 1% solution, the quantity was 40% of the weight of wool, and the dyeing was carried out at 20° for 48 hours. A similar experiment was made taking 1 g. of dye in 75 c.c. of 30% acetic acid; 2·5 g. of wool were dyed at 20° for 24 hours. No activity was noticed at first, but after 72 hours a slight lævorotation was observed. Experiments with wool and silk using alcohol and dilute sulphuric acid as solvent for the dye showed no activity. These experiments on the racemoid dye did not furnish decisive evidence of preferential dyeing with either enantiomorph.

Resolution of dl-4′-*Sulphobenzenedis*-4-*azodiphenyl*-βγ-*diamino*-n-*butane.*—*Brucine salt.* Brucine acetate (2·65 g. or 2 mols.) in 20 c.c. of water was added to 2 g. of the potassium salt of the dye in 50 c.c. of water. The dibrucine salt of the dye separated as a brownish-yellow precipitate (decomposition point 189°); it was moderately soluble in chloroform, but insoluble in other organic media or water. From chloroform alone and from this solvent mixed with light petroleum the brucine salt separated in shellac-like or viscid forms, but not in a crystalline condition (Found: azo-N_2 by titanous chloride, 4·0. $C_{28}H_{28}O_6N_6S_2,2C_{23}H_{26}O_4N_2$ requires azo-N_2, 4·0%). The analysis showed that the substance was a dibrucine salt (2 mols. B + 1 mol. azo-compound).

The *strychnine* salt was prepared from strychnine hydrochloride and the potassium azo-dye salt as in the preceding preparation.

The bright yellow precipitate was readily soluble in chloroform, less soluble in alcohol or acetone, and insoluble in other organic media or water. When a dilute solution in absolute alcohol was allowed to evaporate very slowly, the strychnine salt separated in small needles, decomp. 179° (Found: azo-N_2, 4·4; total N, 11·1, 11·2. $C_{28}H_{28}O_6N_6S_2,2C_{21}H_{22}O_2N_2$ requires azo-N_2, 4·4; total N, 11·0%).

The strychnine salt was crystallised repeatedly from alcohol, the least soluble portions were examined polarimetrically, and crystallisation was continued until the rotation was constant: $[\alpha]^{17°}_{5563} = -308·3°$ for a 0·96% alcoholic solution ($l = 0·5$).

The salt having this specific rotation was warmed gently with aqueous potassium carbonate. The filtrate from strychnine was extracted repeatedly with chloroform to remove any of this base remaining in solution. The aqueous solution was allowed to evaporate, when the active potassium salt of the resolved dye separated slowly. A 0·99% solution gave $\alpha^{17°}_{6563} - 1·02°$ ($l = 0·5$) or $[\alpha]^{17°} = -206°$, $[M]^{17°} = -1409°$. The *l*-potassium salt, like its *dl*-isomeride, was anhydrous (Found: total N, 12·5; azo-N_2, 8·15, 8·2; K, 11·5. $C_{28}H_{26}O_6N_6S_2K_2$ requires total N, 12·3; azo-N_2, 8·1; K, 11·4%).

The mother-liquors from the lævorotatory strychnine salt were examined for the *d*-salt, but the more soluble fractions were viscid and on decomposition with potassium carbonate did not yield any dextrorotatory potassium salt.

Cinchonidine salts. The two stereoisomeric potassium salts were ultimately obtained through the cinchonidine salts. A solution of 2 g. (2 mols.) of cinchonidine hydrochloride in 20 c.c. of water was added to 2 g. of *dl*-potassium salt in 50 c.c. of water, when a yellow precipitate of the cinchonidine salt was obtained almost quantitatively (Found: total N, 11·9, 11·8; azo-N_2, 4·6, 4·7. $C_{28}H_{28}O_6N_6S_2,2C_{19}H_{22}ON_2$ requires total N, 11·7; azo-N_2, 4·7%).

The cinchonidine salt decomposing at 176° was moderately soluble in chloroform or alcohol, slightly soluble in benzene, but insoluble in other organic solvents and in water. By slow evaporation of a dilute alcoholic solution the cinchonidine salt was obtained in small needles and this crystallisation was repeated until the rotation was constant. A 0·97% solution gave $\alpha^{18°}_{6563} - 1·32°$ ($l = 0·5$) or $[\alpha]^{18°}_{6563} = -272°$.

This less soluble salt was decomposed by warming with aqueous potassium carbonate. The filtrate from cinchonidine was extracted repeatedly with chloroform to remove any traces of the alkaloid remaining in solution. The lævorotatory *potassium* salt (0·99% solution) gave $\alpha - 0·87°$, $[\alpha]^{16·8°} = -176·1°$, $[M]^{16·8°} = -1204°$

(Found: total N, 12·4; azo-N_2, 8·1, 8·15. $C_{28}H_{26}O_6N_6S_2K_2$ requires total N, 12·3; azo-N_2, 8·2%).

The dextrorotatory potassium salt. The cinchonidine salt of the dextrorotatory acid was isolated by concentrating the mother-liquor from the foregoing less soluble cinchonidine salt. The more soluble portions were crystallised repeatedly from alcohol until the rotation was constant; a 0·99% solution gave $\alpha - 0·29°$; $[\alpha]^{17°} = - 58·4°$.

The cinchonidine was then set free by aqueous potassium carbonate and the last traces were removed by chloroform. The aqueous solution slowly deposited the dextrorotatory potassium salt; a 0·977% solution gave $\alpha + 0·82°$; $[\alpha]^{18°} = + 167·8°$, $[M]^{18°} = + 1147·8°$ (Found: K, 11·5; azo-N_2, 8·1. $C_{28}H_{26}O_6N_6S_2K_2$ requires K, 11·4; azo-N_2, 8·2%).

The lævo- and dextro-rotatory potassium salts as obtained by the resolution with cinchonidine are in agreement with regard to optical activity, whereas the lævo-salt obtained through the strychnine resolution is more active. These differences, although not entirely explained, are not due to contamination with alkaloids, for these were recovered quantitatively. The resolution was probably more complete in one case than the other.

In the course of the attempts to isolate the dextro-form of the dye the following alkaloidal salts were prepared: *Morphine* salt, brownish-yellow precipitate insoluble in water or organic media, charring at 184°; *codeine* salt, a viscid, brownish-yellow mass more soluble in water than the other alkaloidal salts; *cinchonine* salt, brownish-yellow, amorphous powder fairly soluble in alcohol or chloroform, less so in acetone, but practically insoluble in other media or water; decomposed at 192°.

meso-*Di*-4′-*sulphobenzene*-4-*disazodiphenyl*-βγ-*diamino*-n-*butane*.—This substance was prepared in order to complete the series *dl*, *d*, *l*, and *mcso* of the stereoisomeric azo-acids by adding 0·9 g. (1 mol.) of *meso*-diphenyl-βγ-diamino-*n*-butane dissolved in 1 c.c. of concentrated hydrochloric acid and 5 c.c. of water to a solution of benzene-*p*-diazoniumsulphonate from 1·3 g. (2 mols.) of sulphanilic acid. The dark red *meso*-azo-dye was precipitated (yield 87%). It was slightly soluble in alcohol or glacial acetic acid and almost insoluble in other organic media or water. It was purified through the potassium salt (Found: K, 11·5; S, 9·3. $C_{28}H_{26}O_6N_6S_2K_2$ requires K, 11·4; S, 9·35%).

This *meso*-azo-acid and its salts are more stable and less soluble than the corresponding externally compensated compounds. The *codeine* salt of the *meso*-acid is very insoluble, thus differing from the codeine salt of the *dl*-acid.

Rates of Absorption by Wool of the Stereoisomeric Azo-dyes (*dl*-, *d*-, *l*-, and *meso*-forms).—The experiments with the four stereoisomerides were arranged to run concurrently, the dyeings being carried out in a thermostat at 20°. At intervals of 3, 24, 48, 72, and 96 hours, 5 c.c. of solution were removed and the amount of azo-dye was estimated by titration with dilute titanous chloride. The solutions of the dyes were made in 50% acetic acid.

I. Racemoid form: 2·4642 g. of wool in 100 c.c. of solution with 0·4576 g. of dye.
II. *Dextro*-form: 2·4886 g. of wool in 101 c.c. of solution with 0·4621 g. of dye.
III. *Lævo*-form: 2·4691 g. of wool in 100·2 c.c. of solution with 0·4555 g. of dye.
IV. *Meso*-form: 2·5007 g. of wool in 101·5 c.c. of solution with 0·4644 g. of dye.

Time (hours).	Amount (g.) in 5 c.c. of solution. I.	II.	III.	IV.
0	0·02288	0·02288	0·02288	0·02288
3	0·02276	0·02265	0·02278	0·02277
24	0·02153	0·02144	0·02164	0·02205
48	0·02024	0·02016	0·02033	0·02138
72	0·01923	0·01909	0·01933	0·02081
96	0·01887	0·01866	0·01896	0·02047

These tabulated data show that the dextrorotatory isomeride is absorbed by wool at a consistently though only slightly faster rate than the racemoid form and that the lævorotatory form is absorbed less rapidly than either the *dl*- or *d*-form, which result is in agreement with the polarimetric indications obtained (p. 1736) in the experiments on the selective action of wool on the racemoid azo-dye. A slight development of lævorotatory activity was detected in the dye-bath.

The *meso*-form is absorbed less readily than any of its three isomerides.

The differences in the rates of absorption of the *d*- and *l*-forms show that selective absorption from a racemoid mixture is quite feasible, but in the case of the sulphonated dyes examined in the preceding experiments the differences were not sufficiently large to admit of direct measurements of optical activity. Hence further experiments were made with less acidic carboxylated azo-dyes.

dl-trans-2′-*Carboxybenzene*-4-*azodiphenyl*-βγ-*diamino*-n-*butane* (VI).—An ice-cold solution of benzene-1-diazonium-2-carboxylate, prepared from 5 g. of anthranilic acid (1 mol.), 3·5 c.c. of concentrated hydrochloric acid and 2·5 g. of sodium nitrite in 60 c.c. of water, was added to 4·25 g. (1 mol.) of *dl*-diphenyl-βγ-diamino-*n*-butane dissolved in 15 c.c. of water containing 2 c.c. of glacial acetic acid and 2·5 g. of sodium acetate, when a dark red dye was precipitated.

After 3 hours the coupling was completed by warming on the water-bath. The dye was then collected and washed with ether to remove salicylic acid formed by hydrolysis of the diazonium salt (yield 78%).

Crystallised from 50% acetic acid, the red azo-dye separated in small, dark red needles, decomp. 113°. It was readily soluble in glacial acetic acid, less soluble in methyl and ethyl alcohols, and sparingly soluble in water. It exhibited amphoteric properties, being soluble either in mineral acids or in aqueous ammonia. The atter solution was used in purifying the dye, for on concentration the ammonium salt crystallised. The free acid was subsequently crystallised from glacial acetic acid (Found : total N, 14·6; azo-N_2, 7·1, 7·15. $C_{23}H_{24}O_2N_4$ requires total N, 14·4; azo-N_2, 7·2%). These analyses show that the compound is a monoazo-dye, only one diazo-group being coupled with the diamine.

The monoazo-colouring matter dyed wool in brownish-red shades and silk in dark salmon shades. Experiments were made with this racemoid monoazo-dye with varying conditions as to solvent, time of contact, and concentration of solution as with the racemoid sulphonated disazo-dye, but in no case was there any indication of optical activity.

Resolution of the Racemoid Carboxylated Dye.—The *strychnine* salt was obtained as a red precipitate on adding 1·8 g. of strychnine hydrochloride (1 mol.) in 25 c.c. of water to 2 g. (1 mol.) of the ammonium salt of *dl-trans*-2′-carboxybenzene-4-azodiphenyl-βγ-diamino-*n*-butane dissolved in 50 c.c. of water. This salt dissolved readily in alcohol or chloroform, more sparingly in acetone, but was practically insoluble in other organic solvents and in water. From its alcoholic solution the salt separated on slow evaporation in small needles, decomp. 121° (Found : total N, 11·8; azo-N_2, 3·8. $C_{23}H_{24}O_2N_4$,$C_{21}H_{22}O_2N_2$ requires total N, 11·6; azo-N_2, 3·9%).

Resolution was effected by repeated crystallisation in absolute alcohol until a constant value was obtained for the optical activity; 1% alcoholic solutions were employed with light of wave-length 6708 Å. A 1·02% solution gave $\alpha - 0{\cdot}41°$ ($l = 0{\cdot}5$); $[\alpha]^{19°} = -80{\cdot}5°$. This strychnine salt was decomposed by warming gently with the calculated amount of ammonium carbonate in aqueous solution. The strychnine was precipitated, and the solution extracted repeatedly with chloroform to remove traces of the alkaloid. The filtrate was concentrated in a vacuum at the ordinary temperature until the ammonium salt crystallised. Approximately 1% aqueous solutions of this ammonium salt were examined polarimetrically. A 1·10% solution gave $\alpha - 0{\cdot}24°$; $[\alpha]^{16°} = -43{\cdot}7°$,

whence $[M]^{16°} = -169{\cdot}6°$ (Found: azo-N_2, 6·8. $C_{23}H_{27}O_2N_5$ requires azo-N_2, 6·9%).

Attempts were now made to isolate the *dextro*-form of the azo-compound from the more soluble mother-liquors from the *l*-strychnine salt, but it was found impossible to obtain an even slightly dextrorotatory ammonium salt. Other alkaloids such as brucine, morphine, codeine, cinchonine and cinchonidine did not assist in bringing about this resolution.

dl-cis-2′-*Carboxybenzene*-4-*azodiphenyl*-βγ-*diamino*-n-*butane* (V).—Anthranilic acid was diazotised and coupled with *meso*-diphenyl-βγ-diamino-*n*-butane, when, owing to the circumstance that the diazonium carboxylate coupled with the diamine in molecular proportions, the resulting monoazo-derivative was no longer a *meso*-compound having internal compensation, but was capable of resolution.

The red dye crystallised from 50% acetic acid in small, red needles, decomp. 116°; its solubility and dyeing properties are similar to those of the corresponding *dl-trans*-compound (Found: azo-N_2, 7·15. $C_{23}H_{24}O_2N_4$ requires azo-N_2, 7·2%).

Rates of Absorption by Wool of the Stereoisomeric Carboxylated Azo-dyes.—The experiments were carried out precisely as described on pp. 1732, 1739, excepting that the solutions were made up with 30% acetic acid.

I. *dl-trans*-Form: 5·0116 g. of wool in 200 c.c. of solution with 1·2768 g. of dye.
II. *l-trans*-Form: 5·1334 g. of wool in 205 c.c. of solution with 1·3074 g. of dye.
III. *dl-cis*-Form: 5·0521 g. of wool in 201·6 c.c. of solution with 1·2870 g. of dye.

Time (hours).	Amount (g.) in 5 c.c. of solution. I.	II.	III.
0	0·03192	0·03192	0·03192
3	0·03148	0·03151	0·03150
24	0·02802	0·02929	0·02849
46	0·02503	0·02685	0·02546
72	0·02359	0·02454	0·02377
98	0·02282	0·02337	0·02298
120	0·02253	0·02283	0·02263

The foregoing data showed that the *cis*- and *trans-dl*-forms were absorbed at practically the same rate and that the active lævo-form was absorbed less rapidly than the corresponding racemoid form, the difference in these rates of absorption being rather greater than in the case of the sulphonated azo-dyes.

Note on the Sulphonation of dl-*Diphenyl*-βγ-*diamino*-n-*butane.*

Treatment of this diamine with oleum (up to 20% SO_3) led to hydrolytic decomposition, so that the sulphonated product was

sulphanilic acid. Chlorosulphonic acid also gave rise to complicated reactions and the formation of complex sulphonated sulphones. By neither treatment was a simple sulphonated product of the base obtained, so that the attempt to resolve this *dl*-diamine through its sulphonic acid was abandoned.

The authors desire to express their thanks to the Research Committee of the University of Birmingham and to the Advisory Council of the Department of Scientific and Industrial Research for grants which have helped to defray the expense of this investigation.

UNIVERSITY OF BIRMINGHAM,
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CCXXXI.—*Theories of Polar and Non-polar Free Affinities. A Practical and Theoretical Reply to some Recent Criticisms and Comparisons.*

By GEORGE NORMAN BURKHARDT and ARTHUR LAPWORTH.

IN a paper by C. K. Ingold (J., 1924, **125**, 93) the following sentences occur:

"The establishment of this formula provides an interesting test of the hypothesis by means of which so many obscure points in chemistry are nowadays 'explained.' In nitrosobenzene oxygen is the 'key-atom' (Lapworth, T., 1922, **121**, 416), and the compound may be represented as $C_6H_5-\overset{+}{N}=\overset{-}{O}$."

The sentences are misleading in several ways. As only one reference to the literature is given, it is necessary to point out (1) that Lapworth had never discussed the case of nitrosobenzene and (2) that the phrasing of the second sentence shows that Lapworth's conception of key-atoms is misunderstood. Ingold here, as elsewhere (this vol., p. 514), confuses the conception with the earlier one of Flürscheim. Both theories attribute to bivalent oxygen, for example, a special capacity to affect the properties of the rest of the molecule; Flürscheim's theory, however, postulates a fixed configuration for each compound, and Lapworth's (like that of Kermack and Robinson) does not.

The assumption that all "polarity theories" conform to the same regulations as Flürscheim's is the origin of a number of misdirected criticisms. When the inaptness of this line of attack is realised, the critics substitute the objection that those theories are so flexible as to have no prophetic power in potential test cases (compare C. K.

and E. H. Ingold, this vol., p. 871). This peculiarity merely shows, however, that the cases thought of are not test cases at all. Some real test cases are mentioned later in the present paper.

The doctrine that theories such as those of Thiele and Flürscheim are not so flexible in their application as polarity theories is widely preached, and in view of its reappearance in the paper last mentioned it becomes necessary to prove that it is a fallacious one, in fairness to the theories disparaged.

The theories of fixed non-polar free affinities * certainly give unequivocal and correct correspondence with fact, but only within certain limited ranges. Outside those ranges they show on the same basis an unequivocal disagreement with fact. Thiele's form "explains" the ordinary additive reactions of carbonyl correctly, but on the same principle foretells *o*-*p*-substitution in benzaldehyde. Flürscheim's form explains *m*-substitution in benzaldehyde, but signally fails to explain the additive properties of carbonyl compounds. Flürscheim explains meta-substitution in benzaldehyde by assuming that the agent first attacks the meta-carbon atom; but he explains cyanohydrin formation by assuming that the agent first attacks the oxygen atom (*Chem. and Ind.*, 1925, **44**, 172).

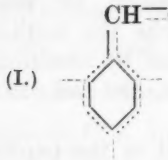
Another excellent example of this is found in the explanation offered for the addition of potassium carbazole to nitrobenzene, where the potassium attaches itself to an oxygen atom and the carbazole residue to the para-carbon atom (*ibid.*, 173): or, looking at it in a slightly different way, Flürscheim here throws over his own formula and adopts Thiele's, its exact opposite. In these systems, therefore, there are nearly always two such possibilities and to quote Flürscheim's words in a similar connexion, "whichever way the experiment goes, one of these alternatives is bound to fit and whichever fits is adopted from case to case" (*ibid.*, 1925, **44**, 84). Such a process of reasoning is, of course, appropriate for the theory which deduces configuration from observed facts, but is not admissible for one which claims to predict facts from *a priori* considerations.

The claim that no arbitrary factor enters into the so-called

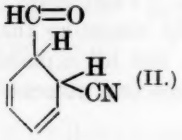
* The description of an hypothesis or a theory such as that of Flürscheim as one of "alternating affinity demand" cannot be used to distinguish it from theories of Kermack and Robinson or Lapworth which also postulate alternating affinity demands. It is necessary, therefore, to protest emphatically against the terminology adopted in the above paper of Ingold and Ingold (*loc. cit.*, p. 870) as likely to spread the perplexity to which one of these authors has frankly confessed (this vol., p. 514, footnote). No question of priority can be admitted as sufficient reason for an implied distinction which does not exist.

predictions of the non-polar theories is therefore one which cannot be taken seriously. No similar claim has ever been made by any responsible exponent of the polarity theories which Ingold discusses. Polarity theories are acknowledged to be in a state of evolution and at present function properly as aids to interpretation, not as substitutes for intellectual effort.

Polarity considerations solve some of the difficulties inseparable from the theories of Thiele and Flürscheim and in a very simple and logical way, because, with a polar agent which has consistent polar selectivity, it is evident that no matter what may be the dominant distribution of affinity in a molecule attacked by that agent, the free affinity will not be effective but rather inhibitive if it is associated with an electrical charge of the wrong sign. Thus, the *dominant* phases of benzaldehyde, so far as activation of the nucleus by the oxygen is concerned, are probably those corresponding with conjugated forms of the Thiele type (I).



(I.)

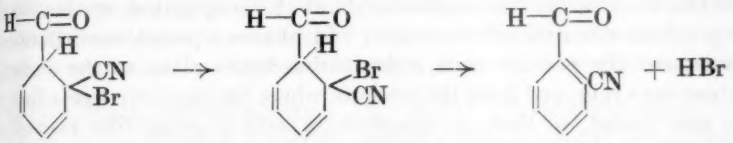


(II.)

This corresponds with Robinson's "crotonoid" forms (*Chem. and Ind.*, 1925, **44**, 456) and the polarities of the excess free affinities in the *o*- and *p*-carbon atoms are mainly positive, as the relation of these positions to the predominating key-atom in the conjugated system shows. The ordinary types of substitution in benzene, such as nitration, sulphonation, bromination, and diazonium coupling require a negative free affinity at the carbon atom at which substitution of hydrogen takes place. Consequently with benzaldehyde, phases of the above type are almost or quite inert towards such agents, substitution is very slow and perhaps takes place only in other phases of rare occurrence in the reacting system.

The circumstance that benzaldehyde is not known to pick up negative ions like cyanidion at the *o*- and *p*-positions in the nucleus, although it does so readily at the carbonyl carbon atom, is not in the least incompatible with the above view. The addition reactions of αβ-unsaturated carbonyl compounds with electrolytes are reversible, and in view of this, as well as the known tendency of dihydro-derivatives to revert to benzenoid types, it is practically certain that the expected addition product (II) is a compound which would not exist in any considerable proportion in equilibrium with benzaldehyde and hydrogen cyanide. By introducing any other conditions which would permit the initial addition compound with

hydrogen cyanide to revert to an aromatic type in a different way, evidence might be obtained of the formation of that compound; such a condition would possibly be provided in *o*-bromobenzaldehyde, as the addition product here could react as follows if *cis-trans* change occurs before reversion :

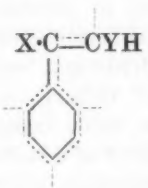


This case would be exactly comparable with the ready replacement of halogen by hydroxyl in the *o*- and *p*-chloronitrobenzenes, which is claimed, not as a prediction from polar theories, but only as part of the evidence in favour of them.

Not less important and obviously very intimately connected with the known reversibility of the negative ion additions to αβ-unsaturated compounds, is the circumstance that tervalent carbon appears to tolerate a positive charge much more readily than it does a negative charge, and $\overset{\oplus}{C}H_3$ has frequently been detected by Sir J. J. Thomson in vacuum-tubes but $\overset{\ominus}{C}H_3$ never. Other things being equal, therefore, positive free valencies on aromatic carbon and on ethylenic carbon appear inert in comparison with negative free valencies.

In the case of phenol ethers, dialkylanilines and many others, the dominant conjugated forms or phases also have their excess free affinities in the *o*- and *p*-positions. Their structures, apart from polarities, correspond with Flürscheim's idea (III),

(III.)



(IV.)

but here the excess free affinities on the carbon atoms in the nucleus are negative; hence ordinary substitution compared with substitution in benzene is very rapid, and certain active positive ions (*e.g.*, diazonium ions) can attach themselves to the active *o*- and *p*-carbon atoms, but never negative ions. Form (III) also corresponds with Robinson's "crotenoid" forms (*loc. cit.*). If the two exterior atoms in (I) are singly bound to each other, conjugation can take place only to that very limited extent which corresponds with the

relatively feeble transmission of alternate polarities through two single bonds.

The third type of conjugation, present in styrene, leads, in the ring, to excess valencies in the *o*-*p*-positions (IV); this obviously facilitates substitution in the nucleus when the excess free affinities in the nucleus are the *negative* ends of the conjugated systems and *o*-*p*-substitution therefore results. In phases where these affinities represent the *positive* ends, substitution takes place at the carbon atom once removed from the nucleus, where the negative free affinity is now found, so that, in competition with a group like carbonyl (and *a fortiori* with a group of the type $-\overset{\cdot\cdot}{\underset{\cdot\cdot}{C}}-\overset{-}{O}R$), which, by conjugation, normally produces only phases with inhibited reactivity towards ordinary substituting agents, the group CX=CYH will normally appear by far the more effective. α-Methoxystyrene provides an instance of such competition within the same side-groups.

The present position is therefore this. Supporters of polar theories accept the general ideas of conjugation and of alternate affinity demand, but do not admit that there is any real distinction between these two conceptions. They hold, however, that these ideas have often been wrongly applied, and have little real predicative power until polar considerations are introduced. It is equally true that the principle of induced alternate polarities is likely to be barren until considered simultaneously with conjugation and other factors; *but this was pointed out in Lapworth's original paper* (*Mem. Manchester Phil. Soc.*, 1920, **64**, ii, 10, last par.) which, it would seem, is rarely consulted.

In the original paper (*loc. cit.*, p. 6), where the general idea of "key-atoms" was broadly indicated, the molecule of formic acid was selected to illustrate that idea. It was explained that in considering different properties of formic acid sometimes oxygen and sometimes hydrogen was considered to be the "key-atom." The "key-atom" in fact, as imagined by Lapworth, is not always the same in the same compound, but is any atom to the alternate inductive effect of which certain properties of the molecule are due. On this conception, the effects of two "key-atoms" may be superimposed—perhaps are always so to some extent—or may so operate that each in turn may determine the properties in different phases of the same molecule (*loc. cit.*). The expression "the key-atom" should be applied only to the atom which is considered responsible for a certain effect and not merely to the one which produces the most striking effects or even to one which has an effect on every property. A suggestion often heard that the introduction of the term "key-atom" merely corresponds with a christening of

Flürscheim's fixed and also non-polarising atom is therefore but a quarter-truth.

It is possible now to return with advantage to Ingold's statement, given at the beginning of the present paper.

As Ingold, with Weaver, has already pointed out (J., 1924, **125**, 1458), there are many close analogies between the addition reactions of the nitroso-group and those of carbonyl. In fact, it may be said that in such cases no evidence has ever been obtained that requires the introduction of the scheme $C_6H_5—\bar{N}=\overset{+}{O}$. In reactions where the oxygen is not directly involved, Ingold's remarks could not in any case apply.

Ingold, however, in the paper first quoted, claimed to have proved that when nitrosobenzene combines with (*a*) methylene-anilines, compounds with four-membered rings are formed, the direction of addition being exactly the opposite of what the usual polarity ideas demand. In the later paper with Weaver (*loc. cit.*) he made similar claims for the reactions of nitrosobenzene with (*b*) hydrocarbons like styrene and diphenylethylene, (*c*) with methylenemalonic ester respectively.

Whilst his later experiments on nuclear substitution in nitroso-benzene and α-methoxystyrene (this vol., pp. 513, 870) introduce no new theoretical difficulties (having given exactly those results which were to be expected), his interpretations of those three types of reaction mentioned in the preceding paragraph are difficult to reconcile with the usual polar additive properties of the compounds. As these interpretations were apparently based on very slender experimental evidence, it was decided to re-examine these three highly interesting cases. The fallacy in case (*c*) has already been detected and may now be dealt with.

Ingold and Weaver (J., 1924, **125**, 1459) found that nitrosobenzene and ethyl methylenemalonate combined to give a crystalline compound. They describe some of the properties of the compound in the following terms: "it gives no colour with ferric chloride, no copper salt, and is oxidised by alkaline permanganate only with difficulty." The constitution ascribed to it was (V) and the formation of this compound was included among the cases in which "the direction of the addition is contrary to the indications of the polar theory." It was maintained that the polarity theory requires the formation of (VI).

(V.) $C_6H_5\cdot N(—O)—CH_2—C(CO_2Et)_2$ $\qquad$ $CH_2(—O—N\cdot C_6H_5)—C(CO_2Et)_2$ (VI.)

The present authors first prepared the product by the same method, but observed that, although no crystalline copper derivatives could

be isolated, with their specimens a strong maroon coloration was always produced when copper acetate was added to an alcoholic solution of the compound.

The compound was a very sensitive one and was rapidly oxidised even in the cold by alcoholic ferric chloride, the odour of nitrosobenzene becoming very perceptible in a minute or two; nitrosobenzene was easily isolated by diluting the resulting solution with water and extracting with ether. Although apparently stable to aqueous permanganate, doubtless owing to its sparing solubility in water, the compound was rapidly oxidised by permanganate in cold acetone. It was evident that the properties of the compound were not consistent with the ring formula previously ascribed to it. As Ingold and Weaver had furnished no direct evidence that the oxygen atom of the nitrosobenzene had taken any part in the act of union, the following experiment was tried :

Ethyl hydroxymethylenemalonate (3 g.) is dissolved in 60% cold methyl alcohol (10 c.c.), β-phenylhydroxylamine (2 g.) is added, when the solid dissolves at once. After 1 or 2 minutes, water is added in sufficient quantity to cause a turbidity. (In the first experiment no crystals were deposited until a trace of the solid, prepared by Ingold and Weaver's method, was introduced, when the whole at once set to a sludge of needles which increased in quantity on further addition of water.) The product (3—3·5 g.) is filtered off, dried, and crystallised from dilute methyl alcohol. The compound so made forms slender needles, m. p. 98—99°, and is identical in all respects (including the intensity and duration of the coloration given in alcoholic solution with copper acetate) with the compound previously described as " ethyl 2-phenyldimethylene-1 : 2-oxaimine-4 : 4-dicarboxylate " (Found : C, 60·0; H, 6·4. Calc., C, 60·2, H, 6·1%).

The compound, then, is one of the possible dynamic isomerides of the *N*-phenyloxime of the ester-aldehyde $O{:}CH{\cdot}CH(CO_2Et)_2$, of which ethyl hydroxymethylenemalonate, $HO{\cdot}CH{:}C(CO_2Et)_2$, is the enolic form. The *N*-phenyloxime of this aldehyde-ester would be $O{:}N(C_6H_5){:}CH{\cdot}CH(CO_2Et)_2$ or, in modernised form, $\overset{\ominus}{O}{\cdot}\overset{\oplus}{N}(C_6H_5){:}CH{\cdot}CH(CO_2Et)_2$. The dynamic isomeride of this corresponding with ethyl hydroxymethylenemalonate is of course $HO{\cdot}N(C_6H_5){\cdot}CH{:}C(CO_2Et)_2$ and it is scarcely possible to state with certainty to which of these formulæ the solid itself corresponds. The behaviour of the compound in alcoholic solution with copper acetate, however, recalls that of the monoalkylated acetoacetic esters, which also give evidence of the formation of dissociable copper derivatives in similar circumstances. It is as likely as not, therefore,

the non-hydroxylic form, or *dicarbethoxymethyl-N-phenylnitrone*, corresponds with the solid and with the one which preponderates in solution. Reference may be made to the work of Alessandri (*Gazzetta*, 1924, **54**, 426) and others on the formation of *N*-phenylnitrones from nitrosobenzene and ethylenic compounds.

On the polarity theory, the first step in the process of union of the ethylenic portion of ethyl methylenemalonate with nitrosobenzene must be the union of the tervalent nitrogen of the nitroso-group with the β-carbon atom of the ester. This carbon atom has a very marked and quite consistent latent or real positive polar character and the first addition process corresponds with ammonium ion formation :

$$\begin{matrix} CH_2{=}C(CO_2Et)_2 \\ O{=}N{\cdot}C_6H_5 \end{matrix} \longrightarrow \begin{matrix} CH_2{-}[C(CO_2\overset{\ominus}{E}t)_2] \\ O{=}\overset{\oplus}{N}{\cdot}C_6H_5 \end{matrix} \quad \text{(VII.)}$$

This initial product (VII) is a bipolar ion (to adopt Lowry's convenient nomenclature), or internal ammonium salt; the signs shown in circles are electrical charges, the positive charge being associated with the ammonium residue; the negative charge is here associated with a residue comparable in every way with the negatively charged organic residue of ethyl *sodio*malonate.

Stabilisation and internal neutralisation of this initial product subsequently occur by "migration" of proton, or exchange of proton with the surrounding molecules in one or more of several possible ways.

The above conclusions are wholly consistent with our knowledge of nitrones, with Lapworth's explanation of the polar additive reactions of αβ-unsaturated carbonyl compounds (J., 1904, **85**, 1212), and with Robinson's interpretation of the polar reactions of nitrosobenzene (*Chem. and Ind.*, 1925, **44**, 456). The formation of addition products of ammonia, and primary and secondary amines, with αβ-unsaturated carbonyl compounds, nitriles, etc., can evidently be explained on very similar lines, stabilisation and internal neutralisation of the bipolar ions in such cases also taking place by a proton migration or interchange, but in a slightly different mode.

It will be instructive for those who have not previously followed the various non-polar theories to their logical conclusions to observe that the β-carbon atom of ethyl methylenemalonate is the one which takes part in the actual union of the molecule of this compound with nitrosobenzene. Now Flürscheim's theory of "orientation" in the aromatic series postulates that the meta-orienting effect of the group of compounds which includes carbethoxyl depends on the assumption that these groups make a smaller affinity demand than

hydrogen, and this results in the development of an excess of free affinity at the meta-carbon atom in the ring, so that the agent attacks the meta-carbon atom preferentially. Applying this argument to ethyl methylenemalonate, it is obvious that replacement of two hydrogens unsymmetrically in the symmetrical ethylene (VIII) by carbethoxyl must lead to the affinity distribution represented by (IX): or, expressed in words, the α-carbon

(VIII.) $CH_2=CH_2$ $CH_2=C<^{CO_2Et}_{CO_2Et}$ (IX.)

atom must have now a greater amount of unbound affinity than the β-carbon atom and therefore the α-carbon atom should be the one at which union with nitrosobenzene takes place: a prediction which fails.

It is not a little remarkable, therefore, that a reaction originally considered to be evidence against the polarity theory provides, when more closely examined, the most elegant known demonstration of the incorrectness of the Werner-Flürscheim theory. Hitherto the most complete disproof would have involved a lengthy mathematical demonstration that it is impossible to construct mass-law equations which shall be capable of explaining the kinetics of the addition of the elements of hydrogen cyanide to cyanoacrylic acids, where the nitrile group corresponds with the carbethoxyl groups (which correspond closely with ethyl methylenemalonate in structure), on any other hypothesis than that the first step in the addition process involves the union of the β-carbon atom with cyanidion (W. J. Jones, J., 1914, **105**, 1547, 1560. Compare also Lapworth, J., 1903, **83**, 995; 1904, **85**, 1208).

All these facts, together with what is known of the conditions of formation and decomposition of the cyanohydrins of simple aldehydes and ketones, show that the revival of the Werner-Flürscheim hypothesis can only have the effect of diverting attention from important issues which have not yet been decided.

Lapworth stated in 1920 that bivalent oxygen is usually more effective than tervalent nitrogen, but the statement had reference to statistical aspects only. Enough is known to show that the dominance of either atom depends on many varying circumstances and the question whether these more frequently favour bivalent oxygen than tervalent nitrogen is not worth debating.

Note added July 12th, 1925.—Compare, on this point, *Chem. and Ind.*, 1925, **44**, 713.

THE UNIVERSITY, MANCHESTER. [*Received, May 16th*, 1925.]

CCXXXII.—*The Estimation of Arsenic in Organic Compounds.*

By GEORGE NEWBERY.

THE most accurate and trustworthy method for the estimation of arsenic in organic arsenical compounds is undoubtedly that in which the arsenic is oxidised by the Carius method to arsenic acid and subsequently weighed as magnesium pyroarsenate. The methods in general use which have been devised in the endeavour to combine the accuracy of this procedure with greater simplicity and rapidity are those of Lehmann (*Apoth. Ztg.*, 1912, **27**, 545) and the modifications suggested by Fargher (J., 1919, **115**, 992) and Myers and Dumez (*U.S. Public Health Rep.*, 1918, **33**, 1003), that of Ewins (J., 1916, **109**, 1355) and of Robertson (*J. Amer. Chem. Soc.*, 1921, **43**, 182). The first of these involves a volumetric determination of doubtful accuracy (compare criticism by Gooch and Morris, *Amer. J. Sci.*, 1900, **10**, 151 and many others); the other two are somewhat tedious in the procedure proposed for the decomposition of the arsenical, and the high temperatures involved render possible some slight loss of arsenic by volatilisation (Myers and Dumez, *loc. cit.*).

The use of ammonium persulphate (in conjunction with nitric acid) for this decomposition has been suggested by Rogers (*Can. Chem. J.*, 1920, **3**, 398) and that of persulphate alone has long been employed in these laboratories. The following process involves this method of oxidation. With the majority of substances to which the method has been applied a determination in duplicate can be completed in the course of an hour: with a few, the boiling down with persulphate has to be prolonged and even repeated with a larger quantity, in order that a colourless solution may be obtained. The decomposition in the case of insoluble substances of acid character is facilitated by solution in caustic alkali before the addition of persulphate, the acid being thus thrown out in a finely divided condition. The details are as follows:—

A mixture of the substance (0·2 g.), 20 c.c. of water, and 4—5 g. of ammonium persulphate is heated to brisk ebullition in a 300 c.c. Erlenmeyer flask, provided with a device to prevent loss by spraying. When the mixture is quite colourless (usually less than 10 minutes is required), 40 c.c. of *N*-oxalic acid are added and the mixture is further heated for 2 minutes after the noticeable evolution of carbon dioxide has ceased. 2*N*-Sulphuric acid (20 c.c.) and 10% potassium iodide solution (10 c.c.) are then added, together with a fragment of porous pot. The mixture is once more vigorously boiled until the

liberated iodine has been almost completely expelled and the solution is of a pale straw colour (about 15 minutes). This colour is discharged by the cautious addition of $N/20$-sodium thiosulphate, the mixture immediately diluted to about 100 c.c., 30 c.c. of $2N$-sodium carbonate are added, and the still acid solution is treated with a quantity of solid sodium bicarbonate about 1 g. in excess of that required to render it neutral to litmus. The mixture is warmed to 35—40° and titrated with $N/10$-iodine in presence of starch solution until the blue colour is permanent.

Appended is a list of some of the results obtained with arsenical products of various types. The figures themselves have not been specially selected and are in all cases duplicate determinations made on the same sample in the ordinary course of work.

Substance analysed.	As% found.	As% calc.
Cacodylic acid	54·5, 54·4	54·3
3-Amino-4-hydroxyphenylarsenious oxide hydrochloride ($1H_2O$)	29·8, 29·8	29·6
Phenylarsinic acid	37·2, 37·3	37·1
p-Tolylarsinic acid	34·8, 34·7	34·7
p-Benzarsinic acid	30·6, 30·5	30·5
p-Arsanilic acid	34·5, 34·6	34·6
3-Nitro-4-hydroxyphenylarsinic acid	28·5, 28·7	28·5
3-Amino-4-hydroxyphenylarsinic acid	31·9, 32·0	32·2
3-Acetylamino-4-hydroxyphenylarsinic acid	27·3, 27·4	27·3
3-Carbethoxyamino-4-hydroxyphenylarsinic acid	24·6, 24·8	24·6
2 : 2′-Dihydroxydiphenylcarbamide-5 : 5′-diarsinic acid	30·6, 30·4	30·5
Sodium *N*-phenylglycineamide-*p*-arsinate (anhydrous tryparsamide)	25·5, 25·4	25·3

	As% found.	As% found by Carius method.
3 : 3′-Diamino-4 : 4′-dihydroxyarsenobenzene hydrochloride (salvarsan)	30·0, 30·1	30·05
Sodium 3 : 3′-diamino-4 : 4′-dihydroxyarsenobenzene-*N*-methylenesulphoxylate (neo-salvarsan)	20·1, 20·2	20·1

RESEARCH LABORATORY, MESSRS. MAY AND BAKER, LTD.
WANDSWORTH, S.W. 18. [*Received, May 20th*, 1925.]

NOTES.

Lithium Arc Spectrum for Polarimetric Use. By PERCY CORLETT AUSTIN.

BY introducing lithium carbonate into the arc produced between carbon, copper, or silver electrodes and using a direct-vision spectroscopic eyepiece of high dispersive power it is possible to read extinctions quite easily, not only for the red line at $\lambda = 6708$ Å. together

with the sodium line at $\lambda = 5893$ Å (Hunter, J., 1924, **125**, 1401), but also for the orange line at $\lambda = 6104$ Å, the blue line at $\lambda = 4602$ Å., and sometimes even the green line at $\lambda = 4972$ Å; but this is much weaker than the others and of comparatively small importance. The red line is very strong and persistent, whilst the blue line is a valuable addition to the list of lines in common use in measurements of optical rotatory dispersion, since it lies in the rather wide gap between the dark blue cadmium line at $\lambda = 4678$ Å. and the mercury line at $\lambda = 4359$ Å. Moreover, it is brighter and more easily read than the dark blue cadmium line, when this is produced in an open arc between electrodes of a cadmium–silver alloy.

The red and blue lines of lithium are widely separated from each other and can be read with sufficient accuracy to enable them to serve as standards, which are independent of the usual mercury lines, in calculating the constants of Drude's equation. The most satisfactory results were obtained with copper electrodes at right angles to each other. The top of the vertical (positive) pole is bound with thin copper wire to retain a small quantity of a paste of lithium carbonate and water, and a current of 4·5 amperes is used. The blue copper lines are too weak to interfere with the readings of the blue lithium line.—WESTMINSTER TRAINING COLLEGE, 130 HORSE-FERRY ROAD, S.W. 1. [*Received, June 16th*, 1925.]

Potassium Antimonoxalate. By LESLIE HENRY ALFRED HOLMES and EUSTACE EBENEZER TURNER.

PRELIMINARY investigation of the antimonoxalates, which it was hoped to resolve into optically active forms, has shown that they are too unstable for the work in view. The potassium salt, for example, is described by different authors as having x, 2, 3, $3\frac{1}{2}$, 4, $4\frac{1}{2}$, or 6 mols. of water of crystallisation (Hofmann, "Lexikon der anorganischen Verbindungen," Vol. I, 2nd half, 1237; Beilstein, "Handbuch," 4th ed., Vol. II, 521).

The potassium salt has been prepared by slowly adding freshly-precipitated antimonious oxide to a boiling saturated solution of potassium hydrogen oxalate, filtering, and allowing to cool: it separated as star-shaped clusters of needles, which were once recrystallised from water below 50° (at or above this temperature it was hydrolysed by water), and air-dried. The water of crystallisation was not completely removed even in a vacuum at 140°, and the determination of water was effected by ignition in a tube, etc. [Found: K, 21·6; Sb, 22·5; C_2O_4, 49·2; H_2O, 6·8. $K_3Sb(C_2O_4)_3,2H_2O$ requires K, 21·8; Sb, 22·35; C_2O_4, 49·15; H_2O, 6·7%).

It is probable that previous workers overlooked the extremely unstable nature of the salt, and were dealing with impure specimens, since it is unlikely that they would have obtained higher hydrates than that now described, which separated at low temperatures.

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A Simplified Method of Micro-combustion: the Micro-Dennstedt Method. By CASIMIR FUNK and STANISLAS KON.

SOME of the disadvantages of Pregl's method of microanalysis have been overcome by Dubsky (see Houben-Weyl, "Methoden der Organischen Chemie," II. ed.), but the apparatus required is somewhat complicated. We have devised a simple and accurate process by an adaptation of Dennstedt's method. The combustions are carried out in a pyrex tube, 43 cm. long, of the usual Pregl pattern, but fitted with an inner tube 22·5 cm. in length, of which 13·5 cm. are inserted into the tube, and a diffusion stopper providing a double supply of oxygen. The filling consists of a platinum contact "star," 6 cm. long, and three boats, 7·5 cm. long, one containing molecular silver and the others lead peroxide and red lead. The tube is heated in a Dubsky furnace terminated by a "regenerating block" kept at 150—170°; the burners are arranged as in the Dennstedt process, so that the contact star can be heated to redness while the portion of the tube containing the absorbents is kept at about 320° with the aid of the tubular burner. Three Blumer absorption tubes, each weighing 14—17 g. when full, are used, filled as recommended by Dubsky; these tubes must always be used in the same direction. A bubble-counter is attached to the third tube. The capillary rubber tubing used for all connexions is specially treated, and the absorption tubes are cleaned and weighed, according to Pregl's directions. It is advisable not to wipe the stoppers after a combustion to avoid the risk of removing small traces of vaselin. The absorption tubes are weighed filled with oxygen and should be refilled with dry oxygen if not used for a day or more.

A newly-fitted combustion tube is burned out in a stream of oxygen for 1½ hours. A small platinum boat containing the substance to be analysed (5—9 mg.) is placed in the inner tube of the combustion tube, the double oxygen supply carefully adjusted, and the combustion carried out as described by Dennstedt. It is particularly important to maintain a sufficiently rapid outer stream of oxygen to prevent backward diffusion of the combustion products,